THE JOURNAL OF GENERAL CHEMISTRY OF THE USSR

Volume 22, No. 3

March, 1952

(A publication of the Academy of Sciences of the USSR)

IN ENGLISH TRANSLATION

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CONSULTANTS BUREAU

152 West 42nd Street,
New York 18, N.Y.

Printed in Great Britain

Annual subscription $95.00
Single issue $12.00

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BERYLLIUM IODOMERCURATES

A. V. Slavvo

The first reports of the preparation of double salts of mercuric iodide and the lower iodides of metals go back to the past century. The production of such compounds is mentioned in the papers by Berthemot, Bonsdorf, and Boullay during the first half of the nineteenth century, and later in papers by Duboin, Dobroserdov, Pavlov, Bogorodsky, and others.

The researches of these authors were chiefly directed to the preparation of new compounds, Dobroserdov being the only one to subject the accumulated experimental material to systematic examination.

According to Dobroserdov [1], all the iodomercurates are salts of two complex acids, $H[HgI_3]$ and $H_2[HgI_4]$, known only in solution. Thus, Dobroserdov reduces all the iodomercurates to two types of salts, $Me[HgI_3]$ and $Me_2[HgI_4]$, Me being an ion of a monovalent metal.

Yet, despite the extensive experimental material dealing with the preparation and study of iodomercurates of the metals of Groups I and II of the periodic system, there is no reference in the literature to the iodomercurates of beryllium. This is the motivation for the present research.

In conformity with Dobroserdov's views, our first experiments aimed at the production and isolation of beryllium tri- and tetraiodomercurates. To secure these salts we prepared a solution of beryllium iodide by dissolving metallic beryllium in strong HI, using 1 gram-atom of Be to 2 moles of HI.

A fresh solution of BeI_2 was saturated with enough anhydrous HgI_2 (two samples being employed) to get salts of the following composition: $Be[HgI_3]_2$ and $Be[HgI_4]$.

Our experiment indicated that in preparing beryllium triiodomercurate the theoretically required quantity of HgI_2 dissolved only when the mixture was heated on a water bath. Cooling the solution to room temperature caused the immediate precipitation of much of the dissolved HgI_2. When the solution was kept in a desiccator over conc. H_2SO_4 a little more HgI_2 precipitated as large, well-formed crystals.

In preparing the $Be[HgI_4]$ salt all the theoretically required HgI_2 dissolved completely in the cold. Both solutions were extremely hygroscopic and unstable when diluted with water. Adding one to two drops of water to 3-5 ml of the solution caused the immediate decomposition of the resultant salt and the precipitation of HgI_2.

It was extremely difficult to establish that a complex salt had been formed in the solution, owing to the solution's excessive hygroscopicity and its instability when diluted with water. Of the existent methods, the only usable ones were the analytic, with the further major restriction that only gaseous reagents could be employed to detect the ions making up the salt, inasmuch as they did not produce any change in the solution concentration. Using nothing but gaseous reagents, we managed to establish the presence of only part of the ions comprising the salt. We were unable to precipitate HgS by using H_2S, one of the most sensitive reagents to the mercury ion, which proved that the mercury was part of a complex ion; NH_3 precipitated beryllium hydroxide, indicating the solution contained free beryllium ions. These tests showed that the solution contained beryllium iodomercurate.

The resultant solutions were kept in a desiccator over H_2SO_4 (sp.gr. 1.84) for about 3 months to secure crystals of the salt. As the solutions thickened HgI_2 gradually precipitated and hydrogen iodide was evolved instead of the expected isolation of the crystals of beryllium iodomercurate, as a result of the decomposition of the complex salt:

$$Be[HgI_4] = HgI_2 + BeI_2;$$

$$BeI_2 + HOH = BeOHI + HI.$$

After 3 months had elapsed, the solutions were transformed into a thick, tacky, dark-brown mass containing crystals of HgI_2 and giving off HI copiously, which was oxidized, in turn, to free iodine.

We were, therefore, unable to recover crystals of beryllium iodomercurate by the method described, though the iodomercurates of the alkali and alkali-earth metals and of magnesium crystallized out rather easily under the conditions specified. Nor did changes introduced into the method of preparation or into the crystallization conditions meet with any success. (A 5% to 15% excess of BeI_2 was added to the solution to lower the solubility of the beryllium iodomercurate, and the solution was concentrated in a vacuum desiccator at the low temperature of 1-2°, 5-10% of hydriodic acid being added to diminish the hydrolysis of the beryllium iodide).

Our subsequent investigations showed that it was possible to isolate the crystals of beryllium iodomercurate when the neutral beryllium iodide was replaced by a basic salt during preparation of the compound. Large green-yellow crystals, in the shape of tetrahedrons, began to settle out of these solutions after 6 to 8 days of concentration over H_2SO_4 (sp.gr. 1.84), no matter what the temperature.

This salt was secured as follows. The basic beryllium iodide was prepared by dissolving enough metallic beryllium to produce BeOHI in 50% HI.

Dissolution, which involved the vigorous evolution of hydrogen at first and considerable warming up of the solution, slowed down so much toward the end of the reaction as to require heating on a water bath. This yielded a thick, heavy, greenish-yellow solution.

Analysis indicated that the solution contained 67.99% BeOHI. This solution was then saturated in the cold with HgI_2, the following proportions being used:

1) 2 Moles of HgI_2 per mole of BeOHI.

2) 1 Mole of HgI_2 per mole of BeOHI.

3) Complete saturation, equivalent to 2 moles of HgI_2 to 3 moles of BeOHI.

Not all of the calculated quantity of HgI_2 dissolved in the first two samples, not even when they were heated on a water bath; hence, solutions of the same concentration – saturated – were secured in all three samples.

Testing the resultant solutions with gaseous H_2S and NH_3 confirmed the formation of beryllium iodomercurate in the solution.

The crystals were thrown down by placing the solution in a desiccator over H_2SO_4 (sp.gr. 1.84) at 15-16°. The solution was partially oxidized during its concentration, turning it a red-brown. Lowering the temperature during concentration diminished the oxidizability of the solution, but did not accelerate crystallization, inasmuch as a drop in temperature had little effect upon the solubility of the salt.

The specific gravity of the solution before crystallization was begun was d^{15}_{15} 3.56. The composition of the mother liquor and of the crystals that settled out of it was determined by chemical analysis.

The following methods were employed to determine composition: the mercury was determined by diluting 0.5 g of the substance with 75-100 ml of water, adding 1 g of $(NH_4)_2SO_4$ or CH_3COONH_4, and passing H_2S through the solution in the cold until it cleared up completely. The mercuric sulfide was filtered through a Schott filter, washed with cold water, and dried to constant weight at 105-106°.

The iodine and the mercury were determined from the same sample. After the mercury had been filtered out, the filtrate was boiled until all the H_2S had been eliminated, the volume of the solution being kept constant. After the solution had cooled, it was titrated with a 0.1 N solution of $AgNO_3$ by the Volhard method.

The beryllium was determined by placing 1 g of the salt in a crucible and carefully heating it to drive off the HgI_2. After the contents of the crucible had cooled, they were moistened with a few drops of concentrated H_2SO_4, the excess of the latter being driven off by heating. The resultant $BeSO_4$ was calcined and then weighed as BeO. The difference in weight was taken as the water. The data on the analysis of the mother liquor are given as per cent in Table 1.

These figures indicate the solution's composition was as follows: $3BeOHI \cdot 2HgI_2 + 7.5\ H_2O$

100 g of the solution contained 91 g of $3BeOHI \cdot 2HgI_2$ at 15°.

Two or three days later a substantial quantity of large tetrahedrons, attached to one another, settled out

TABLE 1

	I	II	III	Mean of 3 determinations
Beryllium.......	1.79	1.74	1.81	1.78
Mercury.........	26.74	26.58	26.69	26.67
Iodine..............	58.95	58.99	59.14	59.03
Water + OH (by difference)	12.62	12.69	12.33	12.55

TABLE 2

	I	II	III	Mean of 3 determinations
Beryllium.......	1.83	1.83	1.85	1.84
Mercury.........	27.14	27.20	27.03	27.12
Iodine...........	60.10	59.98	60.22	60.10
Water + OH (by difference)	10.93	10.99	10.90	10.94

of the solution. The analysis data for these crystals are given in per cent in Table 2.

Analysis indicated that the numbers of atoms of beryllium, mercury, and iodine in the molecule were as follows: 3Be:2Hg: 7I. With these atomic proportions part of the positive valencies of the metallic ions remain unsaturated, the molecule lacking 3 negative ions. In view of the fact that the basic beryllium iodide was used as the initial product in synthesizing this salt, there was reason to assume that the resultant complex molecule also ought to contain hydroxyl groups and that these were the negative ions that saturated the free positive valencies of the metallic ions. Then the composition of the resultant crystals would be best represented by the formula $3BeOHI \cdot 2HgI_2 \cdot 6H_2O$. Comparison of the analytical data with the theoretical evidences good agreement between the two (Table 3).

TABLE 3

	Per cent by analysis	Per cent calculated from the formula
Beryllium.........	1.84	1.83
Mercury............	27.12	27.18
Iodine...............	60.10	60.23
Water + OH (by difference)	10.94	10.77

A direct determination of water by the hydride method [2], made at our request by A.E.Elitsur, the author of that method, confirmed that the molecule of the complex salt contained 6 molecules of water

Properties. The crystals of the salt were greenish-yellow. They were hard and brittle, crumbling readily when pressed with a glass rod. They were highly hygroscopic, adding a minute amount of water causing the immediate decomposition of the salt, with the evolution of HgI_2 at the surface of the crystals. No such decomposition was observed when the salt gradually took up moisture from the air. Tests showed that the addition of two or three per cent of moisture from the air results in dissolution of the crystals, the salt starting to decompose only after 15-17% of water is absorbed.

Neither the external appearance of the salt nor its weight exhibited any change after it had been kept in a desiccator over H_2SO_4 (sp. gr. 1.84) for 5 to 7 days. The salt loses its luster when heated. At 92° the salt begins to decompose, without melting, giving off HgI_2.

Drying the salt in a drying cabinet at a temperature below 70° causes no change in weight, a gain in weight being exhibited at 50-60°. At 85° the salt loses 5.8 to 6.3% of moisture, equivalent to 3.5 to 4.0 molecules of water, the surface of the crystals turning dull. A longer stay in the drying cabinet at this temperature results in decomposition of the complex salt, with the evolution of HgI_2.

The resultant salt is readily soluble in methanol and in ethyl, amyl, and other alcohols. Dissolution involves the decomposition of the complex salt into its initial constituents. The salt is slightly soluble (0.15-0.18%) in benzene, toluene, and chloroform, and very slightly soluble (0.03%) in carbon tetrachloride.

The Coordinate Formula

The stated properties of the salt and, especially, its instability in water and in organic solvents made it extraordinarily difficult to establish its coordinate formula. It was impossible to determine the molecular weight or to establish whether hydroxyl groups were present in the molecule and to determine their position with respect to the central atom.

The comparative ease with which the crystal hydrates of beryllium iodomercurate could be recovered from solutions that contained basic beryllium iodide led us to postulate that the reason for this was a change in the depolarizing effect of the outer sphere due to the appearance of hydroxyl groups within the molecule. The increase in the stability of the complex radical when hydroxyl groups are present in the molecule is evidently due to a weakening of the depolarizing action of the beryllium ions. The diminution of the field of force of the ions in the outer sphere is caused by the partial extinction of the positive valencies of the beryllium ions, due to the addition of the hydroxyl groups. It must be supposed that the divalent beryllium ion adds a single hydroxyl group and becomes monovalent, in which case its polarizing action should differ but little from the action of other monovalent ions with approximately the same radius.

We had to establish the composition of the complex radical to prove that these assumptions were correct. This problem was solved analytically by precipitating the complex ion and making a complete chemical analysis of the precipitate. Three reagents were chosen for this purpose: $CuSO_4$, $AgNO_3$, and $[Pt(NH_3)_4]Cl_2$, in each of which we could expect a double decomposition reaction to result in the formation of a slightly soluble compound containing the complex ion, by analogy with the complex radical $[HgI_4]^{--}$ [3,4,5].

In view of the decomposition of the salt when water is added, these salts had to be synthesized in the dry state; this was done by comminuting the crystalline salts of the initial products in the appropriate proportions (based on the monovalent and divalent complex radicals $-[HgI_3]^-$ and $[HgI_4]^{--}$) until a homogeneous mass was produced, which became moist as the result of its greedy absorption of atmospheric moisture. In each of the three cases the color of the mass changed markedly during comminution.

During the synthesis of copper iodomercurate the iodine ions were partially oxidized to free iodine, large quantities of which were evolved.

The results of our analyses of the reaction products are listed in Tables 4 and 5. The analysis data on copper iodomercurate in Table 4 enable us to establish the simplest chemical formula: $CuI \times HgI_2 \times H_2O$ or $Cu[HgI_3] \cdot H_2O$ (Table 4).

Percent Analysis of Copper Iodomercurate

TABLE 4

	I	II	III	Mean of 3 determinations
Copper..............	9.54	9.57	9.69	9.60
Mercury.............	30.18	30.39	30.36	30.31
Iodine..............	57.72	57.50	57.34	57.52
Water (by differences)...........	2.56	2.54	2.61	2.57

TABLE 5

	Per cent found	Per cent calculated from the formula
Copper...........	9.60	9.59
Mercury........	30.31	30.26
Iodine...........	57.72	57.44
Water (by diferences) ...	2.51	2.71

Percent analysis of tetrammineplatinum iodomercurate (Table 6)

On the basis of the analysis results we have assigned this the simplest chemical formula: $[Pt(NH_3)_4] \cdot [HgI_3]_2$.

TABLE 6

	I	II	III	Mean of 3 determinations
Mercury............	28.34	28.08	28.21	28.21
Platinum...........	13.54	13.77	13.43	13.58
Iodine..............	53.27	53.24	53.51	53.34
Water + NH_3 (by differences)....	4.85	4.91	4.85	4.87

TABLE 7

	Per cent found	Per cent calculated from the formula
Mercury...........	28.21	28.14
Platinum..........	13.58	13.69
Iodine.............	53.34	53.40
Water + NH_3 (by differences)..	4.87	4.76

Percent analysis of silver iodomercurate (Table 8).

The formula $3AgI \cdot 2HgI_2$ or $2Ag[HgI_3] \cdot AgI$ best fits the composition indicated.

The results of analysis lead us to believe that the precipitate of silver iodomercurate consists of two

TABLE 8

	I	II	III	Mean of 3 determinations
Silver............	20.85	21.43	21.63	21.18
Mercury.........	24.70	23.80	23.53	24.01
Iodine...........	54.45	54.73	54.66	54.62
Water (by differences)......	0.40	0.02	0.18	0.20

TABLE 9

	Per cent found	Per cent calculated from the formula
Silver.........	21.17	20.06
Mercury.......	24.01	24.88
Iodine........	54.62	55.07
Water (by differences)	0.21	–

TABLE 10

	I	II	Mean of two determinations
AgI (residue after distillation)	45.94	46.20	46.03
HgI_2 (by differences)	54.06	53.80	53.93
Water (by increase in weight of $CaCl_2$).........	None found		–
	Per cent found		Per cent calculated from the formula $2Ag[HgI_3]\cdot AgI$ (%)
Silver iodide..	46.07		43.66
Mercuric iodide.....................................	53.93		56.36

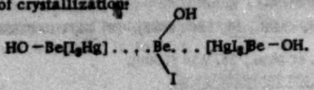
slightly soluble salts, $Ag[HgI_3]$ and AgI, their proportions in the mixture by weight being 2:1.

The foregoing analysis of the silver iodomercurate was paralleled by a simplified analysis of this salt, involving its decomposition into the constituent salts AgI and HgI_2 (this method is founded upon the difference in the volatility of mercuric and silver iodides when heated). The results are given in per cent in Table 10.

The discrepancy between the experimental figures and those calculated theoretically proved that the resultant compound was a mixture. It may be stated, however, that in spite of this discrepancy the simplified method of analysis also confirms the derived formula for silver iodomercurate: $2Ag[HgI_3]\cdot AgI$.

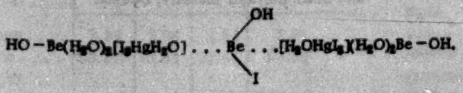
Thus, in all three cases we were able to isolate the complex ion in the precipitate and to demonstrate its composition analytically as $[HgI_3]^-$.

The results of these analyses are grounds for our proposing the following coordinate formula for basic beryllium iodomercurate, ignoring the water of crystallization:



$$HO-Be[I_3Hg]\ldots\overset{OH}{\underset{I}{Be}}\ldots[HgI_3]Be-OH.$$

The following hypothetical distribution of the molecules of crystallization water may be assumed for the crystal hydrate of beryllium iodomercurate:



$$HO-Be(H_2O)_2[I_3HgH_2O]\ldots\overset{OH}{\underset{I}{Be}}\ldots[H_2OHgI_3](H_2O)_2Be-OH.$$

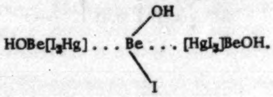
SUMMARY

1. It has been shown that it is impossible to isolate crystal hydrates of beryllium iodomercurate of the following composition: $Me[HgI_4]\cdot xH_2O$ from aqueous solutions, though salts of this composition have been recovered under similar circumstances for all the alkali-earth metals and for magnesium.

In our opinion, the impossibility of isolating the crystal hydrates $Be[HgI_4]\cdot xH_2O$ is due to the high depolarizing effect of the beryllium ion.

2. It is comparatively easy to isolate the crystal hydrate of basic beryllium iodomercurate, which has made it possible to synthesize for the first time the complex salt of basic beryllium iodide and iodomercuric acid $H[HgI_3]$, and to investigate its properties.

3. The coordinate formula of the compound synthesized:



$$HOBe[I_3Hg]\ldots\overset{OH}{\underset{I}{Be}}\ldots[HgI_3]BeOH.$$

was established by the analytical method.

Hence, introducing hydroxyl groups, which partially extinguish the positive valencies of the beryllium ions, into the beryllium iodomercurate molecule diminishes their field of force, weakens their depolarizing action, and promotes the increased stability of the complex ion.

4. During the establishment of the coordinate formula of the basic beryllium triiodomercurate analytically we have synthesized for the first time the copper, silver, and tetrammineplatinum iodomercurates, with the following formulas: $Cu[HgI_3]\cdot H_2O$; $Ag[HgI_3]$ and $[Pt(NH_3)_4]\cdot[HgI_3]_2$.

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Received March 29, 1949.

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BERYLLIUM CHLOROMERCURATES

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Little research has been done on the halogenated compounds of mercury and beryllium. The data encountered in the literature, dealing with the production of chloro- and bromomercurates of the metals in Group II of the periodic system, are evidence of how little work has been done on this problem.

It is stated in the literature that salts of the following compositions: $BaCl_2 \cdot HgCl_2 \cdot 8H_2O$ [1]; $MgCl_2 \cdot 3HgCl_2 \cdot 6H_2O$ [2,3,4] and $BaCl_2 \cdot HgCl_2 \cdot 2H_2O$ [2], have been secured as crystal hydrates, though the preparation of the last salt has not been confirmed by subsequent investigations.

As for beryllium, Bonsdorff is the only one who asserts that the reaction of concentrated solutions of mercuric chloride and beryllium chloride results in the formation of a salt of the composition: $xBeCl_2 \cdot yHgCl_2$. This formula indicates that the author never made a complete analysis of this compound.

In view of the difficulties we encountered in preparing and isolating the crystal hydrates of normal beryllium iodomercurate, due to the high polarizing effect of the beryllium ions in the outer sphere, it might have been thought that the chloro- and bromomercurates of this metal ought to exhibit a higher stability of the complex radical. The radii of the chlorine and bromine ions are smaller than the radius of the iodine ion, and hence the former's lesser tendency to polarization ought to make the complex radicals of the chloro- and bromomercurates more stable, inasmuch as the influence of the outer sphere — the counterpolarizing action of beryllium — ought to be less in these salts. The ease with which the basic salt of beryllium is isolated is due, as we have seen, to a decrease in the counterpolarizing action of the beryllium ions, resulting from the introduction of hydroxyl groups into the outer sphere.

In the light of these considerations we were greatly interested in preparing the normal and basic chloro- and bromomercurates of beryllium in the crystalline state.

Preparation of Beryllium Chloromercurate

The beryllium chloride required in the synthesis of normal beryllium chloromercurate was prepared by dissolving metallic beryllium in 36% hydrochloric acid, the proportions being 1 gram-atom of Be to 2 moles of HCl. The beryllium dissolved violently, large amounts of heat being evolved. We secured a light-yellow solution of $BeCl_2$, the percentage composition of which is given in Table 1.

TABLE 1

	I	II	III	Mean of 3 determinations
Beryllium	2.99	2.94	2.98	2.97
Chlorine	23.29	23.44	23.44	23.39
Water (by differences) .	73.72	73.62	73.58	73.64

Composition of the $BaCl_2 + 12.4H_2O$ solution. 100 g of solution contained 26.29 g of $BeCl_2$ at 15°. A beryllium chloride solution of this concentration was saturated in the cold with $HgCl_2$, 1 mole of $HgCl_2$ being added per mole of $BeCl_2$. This yielded a straw-yellow solution of slight density. The presence of free beryllium ions in this solution was demonstrated by the use of gaseous ammonia, while the action of hydrogen sulfide proved that it contained no mercury ions. These tests confirmed that a coordination compound — beryllium chloromercurate — had been formed in the solution.

The solution was placed in a desiccator at 14-16° together with sulfuric acid (sp.gr. 1.84) in order to concentrate it. Two months later crystals of the salt appeared on the surface of the solution.

The specific gravity of the mother liquor was d_{15}^{15} 3.16 at the instant of crystallization. The solution was analyzed to determine its beryllium, mercury, and chlorine content. The beryllium was determined gravimetrically as BeO, the mercury being determined gravimetrically as HgS, and the chlorine being determined, after the mercury had been precipitated out, by a Volhard titration with a 0.1 N solution with silver nitrate.

This analysis yielded the following results, in per cent (Table 2).

TABLE 2

	I	II	III	Mean of 3 determinations
Beryllium	1.91	1.95	1.94	1.93
Mercury	42.78	42.69	42.74	42.74
Chlorine	30.12	30.29	30.28	30.23
Water (by differences)	25.18	25.07	25.03	25.10

Crystallization was extremely slow. It took two weeks to secure the amount of salt required for analysis. The individual identity of the salt was checked during crystallization by observing the shape of the crystals through a microscope. It should be noted that a separate observation was required to check on the purity of the crystallized salt, inasmuch as we had noted in our work with the iodomercurates that several salts, differing in composition and crystalline form, could be secured in a certain sequence from a single solution during the concentration process. We have observed this phenomenon in the iodomercurates of calcium, barium, lithium, and other metals.

The crystals collected during all this time were square lemon-yellow platelets. These platelets grew together during the process of crystallization, forming clusters. The crystals were lighter than the mother liquor and floated on its surface. The crystals were filtered out of the mother liquor in an atmosphere of dry air and then analyzed, the results of analysis being shown in Table 3.

TABLE 3

No.	Determination of chlorine: Grams of the salt	Determination of chlorine: Ml of 0.1 N $AgNO_3$	Determination of chlorine: Per cent chlorine	Determination of Hg: Grams of HgS	Determination of Hg: Per cent mercury	Determination of beryllium: Grams of the salt	Determination of beryllium: Grams of BeO	Determination of beryllium: Per cent beryllium	Per cent H_2O (by differences)
1	0.3870	35.08	33.14	0.2037	45.37	0.7139	0.0402	2.03	20.46
2	0.3557	32.18	32.08	0.1865	45.24	0.7967	0.0442	2.00	20.68
3	0.4117	37.20	32.04	0.2172	45.48	0.6602	0.0386	2.01	20.47
Average.		32.09			45.36			2.01	20.55
Calculated from the formula: $Be[HgCl_4]\cdot 5H_2O$		32.12			45.44			2.04	20.38

The simplest formula corresponding to the composition indicated by analysis: $BeCl_2 \cdot HgCl_2 \cdot 5H_2O$.

The synthesized salt may be assigned the formula of $Be[HgCl_4]\cdot 5H_2O$, in accordance with the concepts of Dobroserdov [5]. The formation of such a salt is borne out by the negative reaction for free mercury ions.

Properties. Solubility in water at 15°: 95%. The crystals of $Be[HgCl_4]\cdot 5H_2O$ are very hygroscopic. When about 1 gram of the salt was allowed to stand in air of ordinary humidity and temperature, it deliquesced completely within 5-6 minutes. A freshly prepared (1:200) solution of this salt is more stable than a solution of beryllium iodomercurate, no mercury ions being detected during the first 3-5 minutes of passing hydrogen sulfide through the solution, whereas mercuric sulfide is thrown down at once by hydrogen sulfide from a solution that has stood for a while.

$Be[HgCl_4]\cdot 5H_2O$ gradually loses moisture when standing in a desiccator over sulfuric acid (sp.gr. 1.84); the loss of water after 7 days is about 4%, equivalent to 1 mole of water, the surface of the initially transparent and lustrous crystals becoming dull. Keeping the crystals in the desiccator for a longer period caused no further change in weight or in external appearance. The crystals fume slightly when exposed to air, giving off HCl.

Drying at 85° results in a loss of 12.5-13% of the crystallization water, equivalent to 3 moles of H_2O. Further drying at this temperature results in decomposition of the salt, with partial evolution of $HgCl_2$, the salt not melting thereby. $Be[HgCl_4] \cdot 5H_2O$ is readily soluble in methanol and in ethyl and amyl alcohols. It is slightly soluble in toluene, benzene, and chloroform and very slightly soluble in carbon tetrachloride.

Dissolution is accompanied by decomposition of the complex salt into simple chlorides in all these solvents.

Preparation of Basic Beryllium Chloromercurate

The basic beryllium chloride required for the synthesis of basic beryllium chloromercurate was prepared by dissolving metallic beryllium in concentrated hydrochloric acid (36%), 1 gram-atom of Be being used per mole of HCl. Prolonged heating on a water bath was required to dissolve all the beryllium.

The results of analysis of the colorless, heavy solution are given in per cent in Table 4.

TABLE 4

	I	II	III	Mean of 3 determinations
Beryllium	6.36	6.39	6.48	6.41
Chlorine	25.12	25.23	25.26	25.20
H_2O + OH	69.52	69.39	69.39	69.43
(by differences)	69.52	69.39	69.39	69.43

The analysis findings indicated that the solution had the following composition: $BeOHCl + 4.4H_2O$. 100 grams of the solution at 15° contained 43.71 g of BeOHCl.

The resultant solution of basic beryllium chloride was saturated in the cold with mercuric chloride. The following proportions by weight were employed, by analogy with the beryllium iodomercurate we had synthesized previously and in conformity with the concepts of Dobroserdov [5]: 1) 1 mole of $HgCl_2$ per mole of BeOHCl; and 2) 2 moles of $HgCl_2$ per 3 moles of BeOHCl.

All the calculated mercuric chloride dissolved in both cases, no free mercury ions being found in either solution, whereas the reaction for the beryllium ion was positive, indicating that a beryllium chloromercurate had been formed.

When these solutions were concentrated over H_2SO_4 (sp. gr. 1.84) at 15-16°, it took 37 days for crystals to separate out of the first solution and 24 days from the second. The crystals were of the same crystalline form in both cases and, as we later found, of the same chemical composition.

The per cent composition of the first and second mother liquors at the onset of crystallization is given in Tables 5 and 6.

TABLE 5 — Solution I

	I	II	III	Mean of 3 determinations
Beryllium	2.18	2.16	2.16	2.17
Mercury	48.58	48.69	48.83	48.70
Chlorine	25.86	25.65	25.77	25.76
H_2O + OH (by differences)	23.38	23.60	23.24	23.37

TABLE 6 — Solution II

	I	II	III	Mean of 3 determinations
Beryllium	2.91	2.94	2.93	2.93
Mercury	43.84	43.69	43.75	43.76
Chlorine	27.06	27.16	27.03	27.08
H_2O + OH (by differences)	26.19	26.21	26.29	26.23

Composition of Solution I: $BeOHCl \cdot HgCl_2 + 4.4H_2O$. 100 g of the solution at 15° contained 80.70 g of $BeOHCl \cdot HgCl_2$.

Composition of Solution II: $3BeOHCl \cdot 2HgCl_2 + 10.4H_2O$. 100 g of the solution at 15° contained 85.80 g of $3BeOHCl \cdot 2HgCl_2$.

The first and second solutions crystallized differently. The crystals settled out of Solution I gradually, in the course of 4-5 days. A small quantity of crystals settled out of Solution II at once, and three days later the whole solution turned into a solid crystalline mass, adhering solidly to the crystallizer.

The crystals, which were separated from both mother solutions in an atmosphere of dry air, were analyzed, the analysis indicating that they were alike.

The composition of the crystals in the first and second series of tests is given in Table 7.

TABLE 7

Series I

No.	Determination of chlorine			Determination of Mercury		Determination of beryllium			Per cent H_2O + OH (by differences)
	Grams of the salt	Grams of 0.1 N $AgNO_3$	Per cent chlorine	Grams of HgS	Per cent mercury	Grams of the salt	Grams of BeO	Per cent beryllium	
1	0.5098	41.20	28.66	0.3212	54.12	0.9261	0.0814	2.36	14.83
2	0.5067	40.84	28.58	0.3190	54.28	0.8255	0.0545	2.38	14.76
3	0.5459	44.15	28.68	0.3430	54.17	0.7888	0.0538	2.46	14.69
Average			28.64	–	54.19	–	–	2.41	14.76
Series II									
1	0.4375	35.40	28.69	0.2745	54.09	0.7180	0.0480	2.41	14.81
2	0.4739	38.52	28.82	0.2982	54.24	0.6038	0.0408	2.44	14.50
3	0.3744	30.24	28.64	0.2353	54.18	0.7776	0.0552	2.42	14.76
Average			28.72	–	54.17	–	–	2.42	14.69
Calculated from the formula: $BeOH[HgCl_3] \cdot 2H_2O$			28.83	–	54.37	–	–	2.44	14.37

The composition of the crystals as established by analysis was $BeOHCl \cdot HgCl_2 \cdot 2H_2O$ or, by analogy with the beryllium iodomercurate we have synthesized $BeOH[HgCl_3] \cdot 2H_2O$. The synthesized salt may be regarded as a derivative of the acid $H[HgCl_3] \cdot H_2O$.

The water in the crystal hydrates of the beryllium chloromercurates was also determined by the hydride method by A. G. Elitsur, the author of that method [6]. His findings coincided with the percentages of water calculated for these salts by the method of differences.

Properties. The solubility of this salt in 100 g of solution at 15° is 90.0 grams. The crystals were highly hygroscopic; they greedily absorbed moisture from the air, becoming wet very fast. Dissolution in water was slower than with the other halogenomercurates, without any decomposition. A freshly prepared solution (about 1%) exhibited no free mercury ions during the first few minutes after preparation.

In contrast to the crystals of the normal salt, these crystals lost no crystallization water when kept in a desiccator over sulfuric acid.

The crystals suffered a slight loss of weight when kept in a drying cabinet at 60-80°, this loss totaling 0.5%, equivalent to 0.15 molecule of water.

The crystals begin to break down, without melting, when a temperature of 84° is reached.

The basic beryllium chloromercurate behaves like the normal salt in organic solvents.

SUMMARY

1. The crystal hydrates of the beryllium chloromercurates $Be[HgCl_4] \cdot 5H_2O$ and $BeOH[HgCl_3] \cdot 2H_2O$, which may be regarded as derivatives of the chloromercuric acids – $H_2[HgCl_4] \cdot xH_2O$ and $H[HgCl_3] \cdot xH_2O$ have been synthesized for the first time.

2. In contrast to the beryllium iodomercurates, it proved to be possible to isolate the beryllium tetrachloromercurate $Be[HgCl_4] \cdot 5H_2O$. Therefore, the counterpolarizing effect of the outer sphere proved to be weakened, owing to the fact that the chlorine ion has a smaller radius than the iodine ion.

3. A study of the properties of beryllium chloromercurates has shown that the basic salt $BeOH[HgCl_3] \cdot 2H_2O$ possesses a higher stability than either the normal salt $Be[HgCl_4] \cdot 5H_2O$, or the basic beryllium

iodomercurate $BeOHI \cdot 2BeOH[HgI_3] \cdot 6H_2O$.

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Received March 9, 1950

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BERYLLIUM BROMOMERCURATES

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Very little research has been done on the double salts of beryllium bromides and the bromides of other light metals with mercuric bromide. The data in the literature are not always accurate, often requiring further investigation. Until recently not one double salt of the bromides of metals in Group II of the periodic system with mercuric bromide had been isolated in the crystalline state. It is stated in the literature that only in solution have the following salts been prepared: $MgBr_2 \cdot HgBr_2$, $CaBr_2 \cdot HgBr_2$, $BaBr_2 \cdot HgBr_2$ [1], and $SrBr_2 \cdot HgI_2$ [2]. In our investigation of the double halides of beryllium and mercury we have been able to prove experimentally that it is impossible to recover the crystalline double iodides of beryllium and mercury from $BeI_2 \cdot HgI_2$ solutions, owing to the extreme instability of these compounds. The crystal hydrate of the basic beryllium iodomercurate, $BeOHI \cdot 2BeOH[HgI_3] \cdot 6H_2O$, proved to be much more stable. As for the double chlorides of beryllium and mercury, the smaller radius of the chlorine ion made the normal beryllium chloromercurate, which we isolated as a salt with the composition of $Be[HgCl_4] \cdot 5H_2O$, as stable as the basic beryllium chloromercurate, which we isolated as $BeOH[HgCl_3] \cdot 2H_2O$.

The size of the radius of the bromine ion justified the assumption that the stability of beryllium bromomercurates would be higher than that of the iodomercurates and correspondingly smaller than that of the chloromercurates.

These circumstances led us to undertake the present research

Preparation of beryllium bromomercurate was effected by dissolving metallic beryllium in freshly prepared concentrated (40%) hydrobromic acid. Our calculation was based upon the neutral salt, $BeBr_2$. The metal dissolved rapidly, the solution being warmed up considerably. The results of analysis of the colorless solution of beryllium bromide are given in Table 1.

TABLE 1

	I	II	III	Mean of 3 determinations
Beryllium	2.38	2.36	2.45	2.40
Bromine........	42.38	42.53	42.56	42.53
Water (by differences) ...	55.24	55.11	55.00	55.08

TABLE 2

	I	II	III	Mean of 3 determinations
Beryllium......	1.36	1.34	1.38	1.36
Mercury	30.56	30.42	30.36	30.45
Bromine........	48.25	48.32	48.41	48.33
Water (by differences)....	19.83	19.92	19.85	19.87

Composition of the solution: $BeBr_2 + 11.5H_2O$. 100 grams of the solution at 15° contained 44.93 g of $BeBr_2$.

The beryllium bromomercurate was prepared by saturating a solution of beryllium bromide in the cold with mercuric bromide, using 1 mole of $HgBr_2$ per mole of $BeBr_2$.

The resultant solution was not very heavy and was colored a reddish-brown. When it was dehydrated in a desiccator over sulfuric acid (sp. gr. 1.84) at 15°, a small amount of a white precipitate of $HgBr_2$ settled out on the second day; the solution was carefully decanted from this precipitate. As concentration was continued, the color of the solution grew deeper, and large amounts of HBr were evolved. Crystallization set in after three months had elapsed. The specific gravity of the mother liquor was d_{15}^{15} 3.28.

The results of analysis of the solution are given in Table 2.

Composition of the solution: $BeBr_2 \cdot HgBr_2 + 7.2H_2O$. 100 grams of the solution at 15° contained 80.30 g of $BeBr_2 \cdot HgBr_2$.

The crystals were filtered out of the mother liquor in an atmosphere of dry air and then analyzed; the results of analysis are given in Table 3.

TABLE 3

No.	Determination of bromine			Determination of mercury		Determination of beryllium			Per cent water (by differences
	Grams of salt	Ml of 0.1N $AgNO_3$	Per cent bromine	Grams of HgS	Per cent Mercury	Grams of salt	Grams of BeO	% beryllium	
1	0.5600	36.14	51.58	0.2089	32.18	1.1021	0.0428	1.40	14.85
2	0.5807	37.40	51.47	0.2185	32.44	1.2211	0.0481	1.42	14.67
3	0.4779	30.80	51.51	0.1795	32.38	1.3166	0.0504	1.38	14.73
Average			51.52		32.33			1.40	14.75
Calculated from the formula: $Be[HgBr_4] \cdot 5H_2O$			51.62		32.39			1.46	14.53

The analytical findings enable us to represent the composition of the synthesized salt by the formula $BeBr_2 \cdot HgBr_2 \cdot 5H_2O$ or $Be[HgBr_4] \cdot 5H_2O$.

The analytical findings exhibit no significant deviation from the values calculated from the formula.

Properties. The crystals were thin platelets, of the color of bromine water, piled one on top of the other. Like the mother liquor, the crystals fumed when exposed to air, giving off hydrogen bromide. They were 94.70% soluble in water at 15°. The salt was very highly hygroscopic, absorbing moisture from the air and rapidly dissolving. No mercuric bromide was evolved during the process.

Keeping the crystals in a desiccator over concentrated sulfuric acid resulted in a slight loss of weight. The loss of weight totalled some 3% after 3 days, the equivalent of one molecule of water; the surface of the crystals was covered with a slight white film and more hydrogen bromide was given off. The crystals melted in their own crystallization water when they were heated to 30°, decomposing and giving off $HgBr_2$ when heated to 70°. The salt lost about 9% of its water when dried in a drying cabinet, the equivalent of 3 molecules of water. Beryllium bromomercurate is readily soluble in methanol and in ethyl and amyl alcohols, very slightly soluble in toluene and benzene, and practically insoluble in chloroform and carbon tetrachloride. Dissolution in these solvents involves decomposition of the coordination compound into the simple salts.

Preparation of basic beryllium bromomercurate. Basic beryllium bromide was prepared by dissolving metallic beryllium in strong HBr, the proportions being 1 mole of HBr/gram-atom of Be.

The mixture had to be heated on a water bath for several days for all the beryllium to dissolve. The colorless solution was very dense; its percentage composition is given in Table 4.

TABLE 4

	I	II	III	Mean of three determinations
Beryllium	4.27	4.36	4.36	4.31
Bromine	38.27	38.39	38.30	38.32
$H_2O + OH$ (by differences)	57.46	57.25	57.34	57.35

TABLE 5

	I	II	III	Mean of three determinations
Beryllium	2.34	2.30	2.29	2.31
Mercury	34.31	34.43	34.13	34.29
Bromine	47.98	47.77	47.71	47.83
$H_2O + OH$ (by differences)	15.37	15.50	15.87	15.58

Composition of the solution: $BeOHBr + 5.7H_2O$. 100 grams of the solution at 15° contained 50.80 grams of BeOHBr. The basic beryllium bromomercurate was prepared by saturating the prepared solution with mercuric bromide, the proportions used being as follows: 1) 1 mole of $HgBr_2$ per mole of BeOHBr; and 2) 2 moles of $HgBr_2$ to 3 moles of BeOHBr (this ratio of the parts by weight of mercuric bromide and basic beryllium bromide placed in reaction together corresponded to the ratio of mercuric iodide to basic beryllium iodide at which the two combined to constitute the basic beryllium iodomercurate). All the $HgBr_2$ dissolved in the cold in both instances. Both solutions exhibited a positive reaction for the Be ion with gaseous ammonia and a negative reaction for the mercury ion when hydrogen sulfide was passed through the solution. This showed that a beryllium bromomercurate had been formed in the solution.

When the solutions were concentrated in a desiccator over sulfuric acid (sp. gr. 1.84) at 14-16°, they gradually turned brown, taking on the color of bromine water.

Crystals were detected in the second solution after 29 days had elapsed, the specific gravity of the mother liquid being d_{15}^{15} 3.48.

The mother liquid was analyzed, the results being tabulated in per cent in Table 5.

Solution composition: $3BeOHBr \cdot 2HgBr_2 + 7.4H_2O$.

100 grams of the solution at 15° contained 88.70 grams of $3BeOHBr \cdot 2HgBr_2$. The mother liquor was extremely unstable when diluted: the addition of a single drop of water produced the instantaneous decomposition of the complex salt at the point where the water entered, $HgBr_2$ being evolved.

The crystals filtered out of the mother liquor in dehydrated air were analyzed chemically, the results being listed in Table 6.

TABLE 6

No.	Determination of bromine			Determination of mercury		Determination of beryllium			Per cent H_2O + OH (by differences)
	Grams of salt	Ml of 0.1N $AgNO_3$	Per cent bromine	Grams of HgS	Per cent Mercury	Grams of salt	Grams of BeO	% beryllium	
1	0.5181	30.80	47.51	0.2380	39.61	1.4710	0.0702	1.72	11.16
2	0.6135	36.57	47.64	0.2832	39.79	1.0750	0.0540	1.81	10.76
3	0.6578	39.19	47.65	0.3048	39.94	1.0250	0.0506	1.78	10.68
	Average		47.60		39.78			1.77	10.85
	Calculated from the formula: $BeOH[HgBr_3] \cdot 2H_2O$		47.72		39.93			1.79	10.54

The analysis data enable us to represent the composition of the crystals as follows: $BeOHBr \cdot HgBr_2 \cdot 2H_2O$.

The experimental results are in good agreement with those calculated from the formula.

It took much longer for crystallization to commence in the first solution than in the second. Analysis indicated that the crystals recovered from the first and second solutions had the same chemical composition and the same crystalline form. The number of water molecules in the crystal hydrates of the beryllium bromomercurates was also determined by the direct method by A. G. Elitsur, the originator of this method [3]. The results of this determination agreed with the percentage of water in these salts as calculated by the differences.

Properties. The $BeOH[HgBr_3] \cdot 2H_2O$ crystals were light-orange in color. They were hard and brittle, readily crumbling when pressed with a rod. They greedily absorbed moisture from the air, rapidly dissolving, and then decomposing with the evolution of $HgBr_2$.

When the crystals were kept in a desiccator over concentrated sulfuric acid (sp. gr. 1.84), they turned into a solid hyaline mass, though their weight remained unchanged.

The salt began to decompose when heated to 85°, without melting. Keeping the salt in a drying cabinet at a temperature slightly below the decomposition temperature caused a slight loss of weight, 0.5%, equivalent to 0.15 molecule of water.

The basic beryllium bromomercurate behaves like all the other beryllium halogenomercurates in organic solvents.

SUMMARY

1. The crystalline beryllium tetrabromomercurate pentahydrate, $Be[HgBr_4] \cdot 5H_2O$, has been prepared and isolated for the first time by reacting a solution of beryllium bromide with mercuric bromide.

The properties of this hydrate indicate that it may be regarded as the beryllium salt of bromomercuric acid: $H_2[HgBr_4] \cdot xH_2O$.

2. Reacting a solution of basic beryllium bromide with mercuric bromide yields the basic beryllium tribromomercurate, which we have isolated for the first time as a crystal dihydrate, $BeOH[HgBr_3] \cdot 2H_2O$. This hydrate is a derivative of tribromomercuric acid, $H[HgBr_3] \cdot xH_2O$.

3. Comparison of the properties of normal and basic beryllium bromomercurates showed that the basic beryllium bromomercurate possesses higher stability.

4. Comparison of the stability of beryllium chloro-, bromo-, and iodomercurates indicates that the chloro derivative has the highest stability and the iodo one the lowest.

The basic beryllium halogenomercurates are more stable than the normal beryllium tetrahalogenomercurates. As in the normal tetrahalogenomercurates, the stability of the trihalogenomercurates dimishes from chlorine to iodine, which also affects the composition of the basic salts. Whereas the composition of the basic beryllium chloro- and bromomercurates may be represented by the formula $BeOH[HgHa_3] \cdot 2H_2O$, the composition of the basic beryllium iodomercurate isolated under similar conditions is more complex: $BeOHI \cdot 2BeOH[HgI_3] \cdot 6H_2O$.

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Received March 9, 1950.

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ANHYDROUS POTASSIUM METANIOBATE

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Joly [1] produced anhydrous potassium metaniobate by fusing together equimolecular quantities of potassium carbonate, niobium pentoxide, and potassium fluoride, used as a flux.

The first X-ray analysis of anhydrous potassium metaniobate was made by Goldschmidt [2], who showed that $KNbO_3$ has a lattice of the perovskite type with the parameter $a_W = 4.01 \pm 0.02$A. Later, Quill [3] secured a more precise value of the parameter, finding that $a_W = 4.005 \pm 0.02$ A. With this value, we calculated the specific gravity of anhydrous potassium metaniobate as $\underline{d} = 3.634$. There still is no information in the literature on the melting point of $KNbO_3$, its pyknometric specific gravity, or its other constants.

The present research had as its objective the preparation of anhydrous potassium metaniobate by various methods, ascertaining the effect of the methods of preparation upon some properties of the salt, determining its thermal stability at high temperature and its melting point, and finding its pyknometric specific gravity.

Initial Preparations

Niobium pentoxide. A technical mixture "tantalum-niobium" tailings served as the initial raw material for the preparation of pure niobium pentoxide. The mixture contained approximately equal proportions of niobium and tantalum as their fluorides, the principal impurities being compounds of iron, tin, and silicon. The percentage of titanium was negligible. The tailings were processed into pure niobium pentoxide as follows.

A 50-gram batch of the tailings was moistened with water to the consistency of a paste, transferred to a silver cup, and heated with 10 ml of concentrated sulfuric acid until all the hydrofluoric acid had been driven off. Then the entire mass was transferred to a porcelain 1-liter beaker and covered with distilled water, and the mixture thoroughly stirred. The wash waters, which contained large quantities of ferric sulfate, were decanted from the residue. Washing was continued to eliminate all the iron ions and sulfate ions, but it was impossible to eliminate the iron ions completely by this method. The niobium and tantalum oxides, freed of most of their iron, were dried at 120° and then thoroughly mixed with 200 g of a soda-alkali mixture (90% Na_2CO_3 + 10% NaOH). The resultant mixture was sintered in a silver cup; then it was pulverized and treated with cold water, which removed such impurities as tin and silicon, eliminated in the form of stannates and silicates. The alkaline niobates and tantalates produced during sintering remained in the deposit owing to the high alkalinity of the solution. Much of the tin was eliminated from the niobates and tantalates by decanting the alkaline solutions. Not all the tin is eliminated in the shape of stannates at this point [4].

The mixture of sodium tantalates and niobates was dissolved in hot water. The hot solution was treated with hydrochloric acid (1:1), throwing down a voluminous white precipitate of tantalum and niobium pentoxides. The wash waters again exhibited small percentages of iron and tin. All the remaining iron and tin were eliminated by boiling the precipitate with concentrated hydrochloric acid. The mixture of "pentoxides" was washed to remove the traces of hydrochloric acid and then transferred to a lead cup and dissolved in the calculated quantity of 40% hydrofluoric acid. Enough of a potassium fluoride solution was added to the resulting transparent solution to form K_2NbF_7 and K_2TaF_7, plus enough water to keep the acid concentration from exceeding 2%, as indicated by Savchenko and Tananaev [5]. The resulting crystals of potassium fluorotantalate were filtered out on a lead Buchner funnel and washed with a small quantity of cold water. The filtrate and the wash waters, which contained potassium oxyfluoroniobate and traces of potassium fluotantalate, were evaporated to dryness in a lead cup and then heated to 110-120° to eliminate the excess hydrofluoric acid.

To remove all traces of tantalum the crystals of potassium oxyfluoniobate were dissolved in water, the resultant solution being heated on a water bath. To the hot solution there were added 0.5g of hydrofluoric acid and 2 ml of a saturated solution of potassium carbonate. Some time later a minute precipitate of the salt $K_4Ta_4O_5F_{14}$ settled out; it was filtered out. The filtrate was again evaporated to dryness, and the procedure for removing the last traces of tantalum repeated as described above. No more $K_4Ta_4O_5F_{14}$ was found, an indication of the complete separation of the niobium and the tantalum. The potassium oxyfluoniobate was treated with a 10% solution of ammonia in a lead beaker. The precipitated niobium pentahydroxide was washed with water until all the fluorine ions had been eliminated. After drying and calcining, the niobium pentoxide was a white powder that contained no tantalum pentoxide. A text for titanium was negative.

The potassium carbonate employed in this research was marked "c.p."; it was recrystallized, fused in a platinum crucible, and pulverized. The potassium fluoride was prepared from recrystallized potassium carbonate and purified hydrofluoric acid.

Method of analysis. The percentage of niobium pentoxide in the samples of anhydrous potassium metaniobate was determined by fusing a weighed sample of the salt with ten times its weight of ammonium bisulfate and lixiviating the melt with a 5% solution of ammonium carbonate. The sufate ions could then be readily washed out of the niobium pentahydroxide on the filter. The precipitate on the filter was dried, the filter paper incinerated, and the residue calcined in a porcelain crucible to constant weight, the niobium then being determined as the pentoxide. The percentage of potassium oxide was determined by the method suggested by K. L. Malyarov [6].

EXPERIMENTAL

Preparation of anhydrous potassium metaniobate. Three methods are given in the literature [1, 4, 7] for preparing anhydrous potassium metaniobate; all three were used in our research.

a) Pure niobium pentoxide was fused in a platinum crucible with an equimolecular amount of potassium carbonate and potassium fluoride, used as a flux. After the melt had cooled, the crystalline mass was extracted from the crucible and treated with boiling water to remove the potassium fluoride. Microscopic examination readily demonstrated the crystalline structure of the substance produced. The crystals were cubic, resembling the crystals of sodium metaniobate described by Holmquist [8].

Analysis of the crystals yielded the following results:

0.2347, 0.2084 g substance: 0.1718.0, 0.1421 g Nb_2O_5; 0.0630, 0.0560 g K_2O. Found %: Nb_2O_5 73.19, 73.21; K_2O 26.84, 26.82. $KNbO_3$. Calculated %: Nb_2O_5 73.28; K_2O 26.72.

b) Equimolecular quantities of potassium carbonate and niobium pentoxide were thoroughly pulverized and mixed together and then transferred to a silver crucible. The mixture was heated to 800° in a crucible furnace to drive off all the carbon dioxide. The contents of the crucible were then transferred to a beaker containing hot distilled water to eliminate the minute excess of potassium carbonate. After the crystals had been washed and dried, they were examined under the microscope. They resembled the crystals of potassium metaniobate prepared by the preceding method.

Analysis yielded the following results:

0.1983, 0.2008 g substance: 0.1452, 0.1469 Nb_2O_5; 0.0534, 0.0538 g K_2O. Found %: Nb_2O_5 73.23, 73.20; K_2O 26.83, 26.82. $KNbO_3$. Calculated %: Nb_2O_5 73.28; K_2O 26.72.

c) A mixture of niobium pentoxide and K_2CO_3 in the molecular proportions of 1:5 was mixed and melted over a blowpipe flame. The molten mass was cooled and then lixiviated with a small quantity of cold distilled water. As Bedford had found [9] for sodium niobate, this yielded the salt $Na_{14}Nb_{12}O_{37} \cdot 32H_2O$. In the case of potassium niobate the salt was $K_{14}Nb_{12}O_{37} \cdot 28H_2O$. The potassium niobate was filtered out of the mother liquor and dried in air, after which it was transferred to a platinum crucible and calcined for 2 hours at a temperature in excess of 700°. The salt was first dehydrated and then decomposed, forming $KNbO_3$. The resultant potassium metaniobate was water-insoluble. Microscopic examination revealed that the potassium metaniobate retained the 7:6 form of salt crystals (minute, stub prisms).

Analysis yielded the following results:

0.1549, 0.1809 g substance: 0.1133, 0.1325 g Nb_2O_5; 0.0413, 0.0482 g K_2O. Found %: Nb_2O_5 73.15, 73.24; K_2O 26.68, 26.62. $KNbO_3$. Calculated %: Nb_2O_5 73.28; K_2O 26.72.

In view of the fact that there is no information in the literature on the pyknometric determination of the specific gravity of potassium metaniobate, we were interested in learning whether the method of preparing this salt had any effect upon its specific gravity. The specific gravity was determined in a pyknometer with toluene. The test data are listed in Table 1.

TABLE 1

Specific Gravity of Anhydrous Potassium Metaniobate Prepared in Different Ways

	Method of preparing anhydrous potassium metaniobate	Specific gravity
1	Fusing equimolecular quantities of Nb_2O_5 and K_2CO_3	4.596
2	Fusing equimolecular quantities of K_2CO_3, KF, and Nb_2O_5 ...	4.588
3	Decomposing $K_{14}Nb_{12}O_{37} \cdot 28H_2O$	4.586
	Mean value	4.590

According to Windmaisser [7], anhydrous potassium metaniobate decomposes at high temperature, yielding an acid niobate of undetermined composition. His paper makes no mention of the temperature at which the potassium metaniobate decomposes.

We made the following test to determine the melting point of potassium metaniobate and to ascertain its thermal stability at high temperature. A platinum crucible containing 2 g of anhydrous potassium metaniobate was placed in a crucible furnace heated to 1200°. A pyrometer with a platinum-platinum-rhodium thermocouple that had been previously calibrated with $K_2Cr_2O_7$, NaCl, and K_2SO_4 was used to measure temperatures. The potassium metaniobate melted completely at 1200°. One end of the thermocouple, protected by a platinum tip, was immersed in the molten salt. The melting point was determined from the cooling curve. The salt was heated to fusion and the melting point was determined three times. Substituting a corundum crucible for the platinum one made no difference in the shape of the cooling curve or in the melting point of the salt. The melting point of anhydrous potassium metaniobate was found to be 1184 ± 2°.

The cooled melt had a distinctly crystalline structure.

To learn whether potassium metaniobate decomposed at 1200°, the salt was taken out of the crucible and boiled in water. The salt remained insoluble. Analysis indicated its composition was as follows:

0.2013, 0.1890 g substance: 0.1475, 0.1384 g Nb_2O_5; 0.0539, 0.0504 g K_2O. Found %: Nb_2O_5 73.31, 73.23; K_2O 26.79, 26.67. $KNbO_3$. Calculated %: Nb_2O_5 73.28; K_2O 26.72.

The results of analysis show that potassium metaniobate does not decompose when fused.

To ascertain the effect of the method of preparation upon the structure of anhydrous potassium metaniobate we made an X-ray analysis of two samples of $KNbO_3$. The photograph was taken with FeK_α rays.

The diameter of the chamber was close to 57.3 cm, sodium chloride serving as the standard substance. The measurements are listed in Tables 2 and 3.

Comparing the Debye crystallograms, as well as the values of $\underline{d}$, sin θ, and $\sin^2\theta$ listed in the tables, we readily see that they are identical. Calculations indicate that anhydrous potassium metaniobate has a lattice parameter $\underline{a}_w = 4.007 \pm 0.003$A.

The specific gravity calculated by Quill from X-ray data is inaccurate, since he used an atomic weight of 93.3 for niobium.

Substituting the value of the lattice parameter $\underline{a}_w = 4.007 \pm 0.003$ A in the formula for density derived in that paper and taking the atomic weight of niobium as 92.91, we get:

$$d = \frac{1 \cdot 179.92 \cdot 1.65 \cdot 10^{-24}}{(4.007 \cdot 10^{-8})^3} = 4.614.$$

This research demonstrates that the crystalline structure, lattice parameter, and specific gravity of anhydrous potassium metaniobate are unaffected by the method used in its preparation.

TABLE 2

$KNbO_3$, Prepared by Reacting Equimolecular Quantities of K_2CO_3, KF, and Nb_2O_5

FeK_α, λ = 1.932 A, 30 kilovolts, 40 milliamps/g.

No.	hkl	Intensity	1 corrected	a	θ	$\sin\theta$	$\sin^2\theta$	$\sin^2\theta = q(h^2+k^2+l^2)$
1	–	1	12.83	–	12°50'	0.2221	–	–
2	100	10	13.97	4.006	13 57	0.2411	0.05817	1X0.05817
3	–	4	17.75	–	17 45	0.3048	–	–
4	110	10	19.97	2.831	19 57	0.3413	0.11652	2X0.05826
5	111	1	23.68	2.314	24 41	0.4176	0.1744	3X0.05813
6	–	2	25.64	–	25 38	0.4326	–	–
7	200	9	28.85	2.003	28 51	0.4826	0.2339	4X0.05822
8	210	7	32.65	1.791	32 39	0.5394	0.2910	5X0.05819
9	211	10	36.22	1.636	36 12	0.5905	0.3487	6X0.05811
10	220	10	42.97	1.418	42 57	0.6817	0.4647	8X0.05809
11	221	7	46.33	1.336	46 20	0.7234	0.5233	9X0.05814
12	310	8	49.63	1.268	49 38	0.7619	0.5804	10X0.05804
13	311	4	53.05	1.209	53 03	0.7990	0.6384	11X0.05804
14	–	1	55.13	–	55 08	0.8205	–	–
15	322	7	56.65	1.156	56 39	0.8354	0.6971	12X0.05809
16	320	4	60.37	1.112	60 22	0.8691	0.7554	13X0.05811
17	321	10	64.38	1.080	64 23	0.9017	0.8130	14X0.05807

Note: For FeK_α $\sin^2\theta = 0.05813\,(h^2+k^2+l^2)$; $a_w = 4.006 \pm 0.002$ A.

TABLE 3

$KNbO_3$, Prepared by Decomposing $K_{14}Nb_{12}O_{37} \cdot 28H_2O$

FeK_α, λ = 1.932 A, 30 kilovolts, 40 milliamps/g.

No.	hkl	Intensity	1 corrected	a	θ	$\sin\theta$	$\sin^2\theta$	$\sin^2\theta = q(h^2+k^2+l^2)$
1	–	1	12.86	–	12°52'	0.2227	–	–
2	100	10	13.98	4.007	13 58	0.2412	0.05818	1X0.05818
3	–	1	18.33	–	18 20	0.3148	–	–
4	110	10	19.96	2.833	19 57	0.3412	0.11644	2X0.05822
5	111	2	24.70	2.311	24 42	0.4179	0.1747	3X0.05823
6	–	3	26.41	–	26 25	0.4449	–	–
7	200	8	28.84	2.002	28 50	0.4824	0.2327	4X0.05817
8	210	8	32.63	1.791	32 38	0.5391	0.2907	5X0.05814
9	211	10	36.22	1.634	36 13	0.5909	0.3491	6X0.05819
10	220	10	43.03	1.415	43 02	0.6824	0.4657	8X0.05821
11	221	6	46.33	1.335	46 20	0.7233	0.5232	9X0.05813
12	310	8	49.73	1.266	49 44	0.7630	0.5818	10X0.05818
13	311	5	53.14	1.207	53 08	0.8001	0.6402	11X0.05820
14	–	10	54.32	–	54 19	0.8123	–	–
15	222	10	56.72	1.155	56 43	0.8360	0.6983	12X0.05819
16	320	3	60.42	1.111	60 25	0.8697	0.7563	13X0.05818
17	321	8	64.50	1.076	64 30	0.9026	0.8148	14X0.05815

Note. For FeK_α $\sin^2\theta = 0.05818\,(h^2+k^2+l^2)$; aw = 4.007 ± 0.003 A.

SUMMARY

1. **Anhydrous potassium metaniobate, produced in three different ways, has been investigated.**

2. The melting point of anhydrous potassium metaniobate has been found to be 1184 ± 2°.

3. It has been proved that anhydrous potassium metaniobate does not undergo decomposition when fused.

4. It has been found that the crystallographic habit of anhydrous potassium metaniobate varies with the method of preparation.

5. It has been shown that the unit cell of the space lattice of anhydrous potassium metaniobate belongs to the cubic system, no matter what the method used in its preparation, with a lattice parameter of $a_W = 4.007 \pm$ ± 0.003 Å.

6. The specific gravity of anhydrous potassium metaniobate is 4.590 as determined pyknometrically in toluene, this figure being close to the value of 4.614 derived from the X-ray measurements.

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Received June 17, 1950.

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THE DENDRITIC CRYSTALLIZATION OF VARIOUS SALTS FROM AQUEOUS SOLUTIONS

I. THE FORMATION OF DENDRITIC CRYSTALS OF NH_4Cl, KCl, AND NaCl AND THEIR MODIFICATION BY VARIOUS IMPURITIES

Yu. Ya. Tilmans

In a series of previous papers [1] the author has investigated the features involved in the production of dendritic forms of growth of crystals of NH_4Cl and NH_4Br and the modifying action of traces of ions of various metals upon the habit of these crystals. He found that the presence of various cations in the solution always produces the same sequence of changes in the crystal habit of NH_4Cl and NH_4Br.

Under ordinary conditions these substances crystallize only as treelike formations—dendrites. It is impossible to secure crystals of these salts with regular faces no matter how the physical conditions of crystallization (degree of solution supersaturation, solution viscosity, or rate of temperature drop) are varied.

Gradually adding impurities of various ions to the solution produces a change in the external faceting of the crystals. Instead of dendrites, we get crystals of stellate, four-petaled, four-sectored, and finally cubic form, depending upon the concentration of the impurity. Even when the effect of the impurity is slight, yielding only imperfect, intermediate crystalline forms, the sequence of habit changes persists. A sharp change in the habit of the crystals, namely, a change from dendrite to cube, is attained after a certain percentage of the impurity of the given ion has been added at the given temperature.

The molar concentration of cations in solution required for a sharp change in faceting is an index of the intensity of the effect of the ion upon the external faceting of the crystals.

The hypothesis, based upon the results of research, that a given percentage of one impurity may be replaced by a corresponding ("equivalent") percentage of another was also tested in the crystallization of ammonium chloride and bromide in the presence of traces of various pairs of ions ($Fe^{+++} + Ni^{++}$, $Fe^{+++} + Co^{++}$, $Fe^{+++} + Cd^{++}$, $Ni^{++} + Ca^{++}$, and the like).

The results of these tests showed that the action of any percentage of any one impurity in a solution may be supplemented by a certain quantity of another, corresponding to the required concentrations of each of these ions when they act independently upon the faceting of crystals.

When the temperature drop used in crystallization is made steeper, and, hence, the change in the degree of supersaturation with time becomes more rapid, the action of impurities grows weaker, a higher impurity concentration being required for achieving a sharp change in the crystal habit. Further research on the effect of various ions as impurities in the solution has yielded similar results. The homotypy of the action of several ions upon the crystalline form of NH_4Cl and NH_4Br, the identical sequence of formation of the same series of crystalline forms in every instance, and the additivity of the action of these impurities lead us to conclude that the faceting of crystals is influenced by a single factor, related to the orienting field of force of the given ion and to its adsorption at the active centers on the various faces of the crystals.

In the ions tested as impurities the intensity of their action upon crystal form rises parallel with the increase in the ion's field of force, and the impurity concentration required to produce a given effect—the transition from the dendrite form to the cubic form of the crystals—diminishes accordingly. As to the reasons for the dendritic crystallization of various substances from a melt or from solution, they are unknown at the present time.

According to Lehmann [2], the crystallization of salts from solution as dendrites involves a locally repetitive change in concentration. The solution is periodically rendered poorer in nutrient material in the layers directly adjacent to the nascent seed crystals, owing to the increased rate of deposition of the substance. With the emergence of density differences in various layers of the liquid, convection and diffusion currents begin to level out the concentration throughout the liquid, again making the solution supersaturated, again intensifying the deposition of the substance, and forming dendritic branches.

A similar change in concentration and the formation of dendrites takes place during crystallization from the molten state, owing to the liberation of the latent heat of fusion by the nascent crystals, which, in turn, causes a transitory superheating of the liquid in the proximity of the crystals and hence, a retardation of crystallization. After the heat has been dissipated to the surrounding layers, increased crystallization resumes.

A. V. Subnikov [3] believes that the uneven diffusion of the substance into various parts of the crystal whenever the viscosity of the solution is high is the major reason for the production of dendritic forms. The edges and vertices of the crystals obtain much more of the nutrient material than do the faces.

V. D. Kuzbetsov [4] maintains that the presence of impurities in the solution is the cause of dendrite formation.

Petrov and Bukhanova [5], employing the Gibbs-Curie-Wulff principle (of minimum surface energy) and the Bravet principle (of maximum reticular density), regard the formation of dendrites in crystallization from molten metals as due to the higher surface energy of the crystal's vertices and edges, compared to that of its faces. The unlike tendencies of different metals to form dendrites is attributable, in the opinion of these authors, to the very nature of the crystal, its lattice structure.

Opinions also differ as to what a dendrite is. Some researchers (Bochvar, Tammann, etc. [6]) maintain that a metallic dendrite is a treelike crystal growing out of a single center.

Other authors, such as Oknov and Gaev [5] believe that dendrites are junctions of separate crystalline aggregates, oriented in a certain way because of various factors (heat transfer, field of force, etc.).

According to Slavinsky [5], a dendrite is a twinned formation, growing simultaneously along three axes.

The present research has as its objective a study of the conditions governing the constitution of dendritic forms during the crystallization of various salts from solution and the feasibility of modifying these forms when various impurities are present. We have chosen ammonium, sodium, and potassium chlorides as subjects of investigation, the first crystallizing solely in dendrites under ordinary conditions, the second exhibiting a tendency toward dendritic crystallization, and the third exhibiting these forms only under exceptional conditions.

EXPERIMENTAL METHOD

Solutions of NH_4Cl, NaCl, and KCl, saturated at various temperatures, were employed in our crystallization tests. Gelatin, agar-agar, glycerol, and alcohol were added portionwise to identical volumes of these solutions, after which a drop of the solution was spread in a thin layer on a glass slide and examined under the microscope. The impurity was added until the precipitated crystals were predominately dendritic. Then drops of impurity solutions – $FeCl_3$, $CoCl_2$, $NiCl_2$, etc. – were added to these solutions a drop at a time, and the step-by-step reverse transition from the dendritic forms to the initial forms characteristic of these substances was observed microscopically.

The several stages of the dendritic growth of the crystals were photographed.

EXPERIMENTAL

Dendritic crystallization of KCl. 1. KCl crystallizes from aqueous solutions as well-defined cubes. When a drop of an unsaturated solution or a thin layer of the solution on a glass slide is observed under the microscope, we can follow the evolution of dendritic forms (Fig. 1). A square platelet is formed at first, which grows irregularly. A dendrite rapidly develops at one or two vertices of this crystal. 1)

2. 5 ml of a 1% solution of agar-agar was added to 20 ml of a 10% solution of KCl. The solution was stirred as it was heated to 50°. Then a drop of the solution was placed on a glass slide and slowly evaporated, the temperature of the surroundings being 20°.

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1) See plate page 609.

KCl crystallized from such a solution chiefly in the shape of fine branched dendrites, growth usually beginning at the periphery of the drop, the major axis of the dendrite rapidly shifting to the center of the drop, where a few crystals of regular shape settled out. As evaporation continued, a fine network of dendrites also developed between the cubes at the center of the drop. Dendrites were often observed to grow out of the vertices of the cubic crystals (Fig. 2).[*)]

3. We used 15% and 20% KCl solutions and a solution saturated at 50°, adding 5 ml of agar-agar to each. The crystallization conditions were the same as before.

Microscopic examination disclosed that the higher the temperature drop of KCl crystallization, the harder it was for dendritic forms to arise. We were unable to secure crystals of predominately dendritic form from solutions that were saturated at temperatures only slightly above room temperature.

4. A series of dilute KCl solutions was tested. Drops of solution were slowly evaporated on a glass slide. The lower the concentration of the solution, the fewer regular cubes settled out; then the cubes vanished completely, and crystallization involved nothing but fine, highly branched dendrites.

As the solution concentration was diminished, the percentage of agar-agar required to produce a fully dendritic picture likewise decreased. The gradual addition of agar-agar as an impurity produced a transition from the cube to the dendrite. As a rule, the rupture of the correct form began at vertices of the cube, often at several vertices at once (Fig. 3, a,b).[*)]

As the concentration of agar-agar in the KCl solution was raised, the cubic crystals disappeared completely, nothing but dendrites settling out and becoming finer and finer and more and more highly branched. A 10% concentration of agar-agar in the solution produced a wholly dendritic crystallization of KCl.

5. Glycerol was tested as an impurity, the crystallization conditions remaining the same. The presence of glycerol heightened the tendency of KCl to develop dendritic forms, but no fine dendrites appeared even when the glycerol concentration in the solution is high.

The gradual transition from the cubic form to the characteristic dendritic form when glycerol was present is exhibited in Fig. 4, a,b,c.[*)]

When KCl was crystallized from solutions saturated at 50° and above, which contain glycerol, elongated rodlike crystals settled out (Fig. 5).[*)]

Conversion of the dendritic crystal forms to the cubic under the influence of admixtures of $FeCl_3$, $NiCl_2$, and $CoCl_2$. The powerful effect of the presence of Fe^{+++}, Co^{++}, and Ni^{++} ions in the solution upon the habit of NH_4Cl and NH_4Br has been referred to above, the dendrites being gradually converted into cubes.

In the present research we have studied the effect of the same impurities upon the habit of KCl in solutions to which enough agar-agar had been added to develop dendritic forms.

Effect of Fe^{+++}. We used 20 ml of a 10% solution of KCl + 5 ml of a 1% solution of agar-agar. Drop by drop we gradually added 0.273 mole of $FeCl_3$ per liter as an impurity. The crystallization conditions remained the same as before.

The dendritic form gradually vanished at the center of the drop. The dendritic branches grew thicker, becoming faceted at their ends, the number of branches diminishing, with, finally, only first-order axes left. When more of the impurity is added, well-formed crystals of KCl are formed.

The reverse transition from the dendrite to the cube takes place in the order shown in Table 1.

Individual stages of the reverse transition from the dendritic form to the cubic are shown in Fig. 6, g, h.[*)]

Effect of Ni^{++}. The crystallization conditions were the same as before. An admixture of an $NiCl_2$ solution was added a drop at a time to a solution of KCl containing agar-agar. The first few drops of $NiCl_2$ caused no noticeable changes: the dendritic crystals retained their shape. As the concentration of the impurity in the solution increased, deformed polyhedra appeared at the center of the drop, with dendrites growing out of their vertices (Fig. 7).[*)]

A further increase of the $NiCl_2$ concentration in the solution decreased the number of dendrites. Individual dendrites could be seen at the center of the drop, growing out of the crystal vertices, with their branches

[*)] See Plate, page 609.

TABLE 1

Concentration of impurity, millimoles/liter	Change in crystal habit
0.5	Large number of fine dendrites, some cubes, from whose vertices dendrites grow (Fig. 6, a,b).[*]
8 7	The number of dendrites drops. The ends of the branches become faceted. Large number of square platelets and cubes (Fig. 6, c,d). [*]
30	Only the thickened first-order axes are left of the dendritic form, exhibiting only stubby, faceted growths instead of the lateral branches; some platelets and cubes (Fig. 6, e).[*]
41	No dendrites, large number of true cubes and platelets. Only in rare crystals is there still a tendency toward the growth of dendrites from their vertices (Fig 6, f). [*]

acquiring facets at their tips. When the concentration of $NiCl_2$ in the solution reached 178 millimoles per liter, the dendrites vanished.

Effect of Co^{++}. Adding $CoCl_2$ to a KCl solution containing agar-agar produced a similar result. All the dendritic forms disappeared when the concentration of the impurity in solution was 194 millimoles per liter.

Dendritic crystallization of NaCl. NaCl crystallizes from an aqueous solution as cubes, no matter what the temperature drop of crystallization. The dendritic forms appear only when a thin layer of solution, produced by simply immersing a glass slide in the solution, is evaporated. This produces skeletal forms. Quicker evaporation of the drop by means of an air jet, with the resulting rapid change in the degree of supersaturation, causes the usual dendrites to form.

Effect of the admixture of agar-agar. We added 10 ml of a 1% solution of agar-agar to 20 ml of an NaCl solution saturated at 25°. The temperature of the surrounding environment was 20°. Dendrites began to grow at the edges of the drop, cubes and square platelets settling out at the center, after which the intervening space filled up completely with thin, finely-branched dendrites. Dendrites grew out of the vertices of several cubes, as in the case of the KCl.

When glycerol was present, the NaCl crystallized in forms resembling those found in the KCl (Fig. 4).[*] The addition of ethyl, butyl, or isoamyl alcohol promotes the crystallization of the NaCl as elongated rodlike crystals.

Conversion of the dendritic form of NaCl into the cubic when admixtures of $FeCl_3$, $NiCl_2$, or $CoCl_2$ are present. Numerous tests have shown that admixtures of Fe^{+++}, Ni^{++}, and Co^{++} in the solution cause a step-by-step conversion of the dendritic form into the cubic at a certain concentration of the admixture.

The limiting admixture concentrations that cause the total conversion of the NaCl dendrites into cubes are lower than in the crystallization of KCl.

Dendritic crystallization of NH_4Cl and the effect of impurities upon the faceting of the crystals. Ammonium chloride always crystallizes from aqueous solutions in dendrites, no matter what the crystallization conditions may be. At gradual temperature drops and, hence, slight changes in the supersaturation conditions with time and low crystallization rates, the dendrites are formed in the following sequence (Fig. 8).

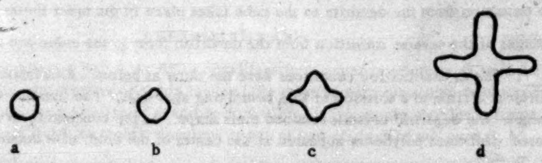

Figure 8.

At first we see a spherical crystal being formed within the field (a). When the crystal has reached a certain size, we see it turning into a rounded square (b), and then into a star (c), the tips of which grow rapidly to form a cross (d) with rounded ends. These microscopic observations can be made by evaporating a drop of the solution slowly on a glass slide.

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[*] See plate, page 609.

When the degree of supersaturation and the crystallization rate are high, finely-branched dendrites are observed. The first-order axes of these dendrites, shaped like sharp arrows, travel rapidly from one edge of the drop to another. Side branches grow simultaneously, but at a slower rate, most often at right angles to the first-order axis.

The addition of various amounts of agar-agar, or ethyl, butyl, or amyl alcohol produced no change in the dendritic forms.

The admixture of $FeCl_3$, $NiCl_2$, or $CoCl_2$ to a solution of NH_4Cl, whether pure or containing various percentages of agar-agar, gradually modifies the shape of the crystals. As the admixtures are added, the usual dendrites are replaced by large arrows, crosses, smaller crosses, rosettes, four-pointed stars, thickened platelets of not quite regular shape, square platelets, and, finally, cubes (Fig. 9).

The concentration of $FeCl_3$ required to convert the dendrites of NH_4Cl into cubes when agar-agar was present was 131 millimoles per liter, or more than when the NH_4Cl was pure (64 millimoles per liter).

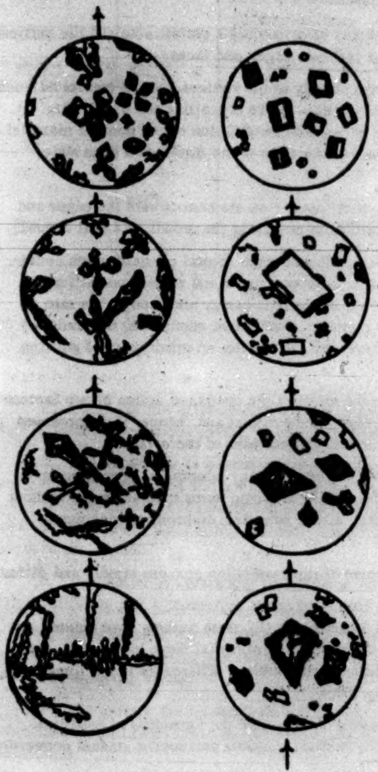

Figure 9

EVALUATION OF RESULTS

1. A detailed study of the conditions governing the crystallization of ammonium, sodium, and potassium chlorides enables us, first of all, to assert that the dendrites of these substances are treelike single-crystal formations, growing out of a single center. This is true both of the formation of a branched dendrite from a seed crystal and of the numerous instances of the growth of dendrites from the vertices of fairly large cubic crystals.

2. The three salts we have investigated differ greatly in their tendency to crystallize in dendritic form. Ammonium chloride yields nothing but dendrites, from a pure aqueous solution as well as when impurities such as agar-agar, glycerol, or alcohol are present.

Potassium chloride forms dendrites under specific crystallization conditions, most readily in the presence of agar-agar, gelatin, and other substances that increase the viscosity of the solution.

Sodium chloride exhibits a lesser tendency to form dendrites, but dendrites are formed when this salt is crystallized from thin solution layers or when an admixture of agar-agar is present.

When it is remembered that many other salts form dendrites under certain conditions, it may be stated that the only role of admixtures of substances that increase the viscosity of the medium and hamper the diffusion of the nutrient material into the growing crystal is to increase the inherent tendency of salts toward dendritic crystallization. This is borne out by the formation of dendrites in sodium chloride.

Considering the separate stages involved in the formation of a dendrite from a cubic crystal of NaCl or KCl, we find that growth occurs chiefly at the vertices of the crystal, as is observed very often in many other substances.

At first, true cubes grow out of the solution drops. When they have reached a certain size and the nutrient material is diminished, uneven surface energy develops at the vertices, edges, and faces.

The uniform growth of the crystal ceases, growth occurring chiefly at the vertices and the regions adjacent to them. The individual stages of dendrite formation are readily visible in the crystallization of KCl (Fig. 1), since its rate of growth is low. This phenomenon is reinforced by nonuniform diffusion of the nutrient material in a viscous medium (in our experiments, by crystallization from a thin layer of the liquid on a glass slide, or in the presence of agar-agar).

As A. V. Shubnikov has shown in his paper [3], the lines of diffusion flow are bent toward the edges and vertices, with their density higher at these points, under any conditions governing the growth of a real crystal.

It may be stated, however, that this nonuniformity is not significant under normal crystallization conditions. As the viscosity of the medium rises, crystal growth begins to depend, more and more, upon diffusion and the preferential access of the nutrient material to its vertices, the surface energy and, hence, the rate of growth of which are greater than that of other elements of the crystals. Under these conditions, the tendency of the substance toward dendritic growth is reinforced. The crystal has, as it were, an opportunity of growing rapidly only as lanceolate, treelike formations.

We may therefore conclude that dendritic forms arise as the result of the combined action of two factors: the relative increase in the surface energy at the vertices and edges of the crystal and, hence, their increased rate of growth, and the uneven diffusion of the nutrient material into various parts of the crystal.

The first of these two factors is an inherent property, more or less, of many substances, depending upon their lattice structure. That is why some substances readily give rise to dendritic forms spontaneously, without any external influence (ammonium chloride and bromide, potash, alum, potassium dichromate, and many others).

Other substances display this tendency only when the degree of supersaturation changes rapidly and diffusion is hampered.

3. In the papers by Rebinder [7], Semenchenko [8], and Serb-Serbina [9], these authors have pointed out that surface-active substances promote fineness of structure and modification of crystal form in metallic and nonmetallic systems. The crystal habit undergoes certain changes as the result of differences in the linear rate of crystallization at various edges, due to the adsorption of impurities.

In the tests we ran, admixtures of agar-agar or glycerol merely accelerated the formation of dendrites. The subsequent addition of admixtures of $FeCl_3$, $NiCl_2$, or $CoCl_2$ to these solutions produced a gradual conversion of the dendrites into cubes via a series of intermediate forms.

The dendritic forms vanish completely at a certain concentration of the impurity in the solution.

A comparison of the limiting concentrations of impurities that produce a conversion of a dendrite into a cube (Table 2) indicates that the greater the tendency of a salt to form dendrites, the higher the ion concentration required to break up the dendritic forms and give rise to well-defined cubes.

We can arrange these impurities in order of decreasing effect upon the faceting of crystals as follows: $Fe^{+++} > Ni^{++} > Co^{++}$, corresponding to the fields of force of these ions.

These results lead us to assume that the active centers of the crystal's surface are charged negatively when one of the ions (in our case, the Cl^- ion) is present in excess, resulting in the adsorption of the cations, Fe^{+++}, Ni^{++}, and Co^{++}.

Adsorption is most intensive at the crystal vertices. This eliminates the preponderant growth of the vertices, and the dendritic form cannot develop. Detailed microscopic examination of all stages of the formation of crystalline forms when these ions are present offers convincing proof of these hypotheses of ours.

When the concentration of the impurity in the solution is below the boundary level, square platelets settle out of the solution and gradually begin to grow. At a certain instant the corners of the square begin to be drawn out, so that further growth yields something approaching a dendritic form. The addition of some more of the impurity gradually offsets this tendency, the growth of the corners being suppressed by the impurity and, finally, cubic formations being produced.

It should likewise be noted that breaking down the dendritic forms produced in the presence of agar-agar or glycerol requires a higher concentration of the impurity ions than when the dendrites are formed without these substances present. This is evidence that agar-agar and other substances increase the tendency of salts to produce dendritic forms at a given concentration in solution.

TABLE 2

Crystallizing salt	Impurity	Limiting concentration of impurity causing a dendrite-cube conversion, millimoles/liter
NH_4Cl	$FeCl_3$	131
	$NiCl_2$	–
	$CoCl_2$	–
KCl	$FeCl_3$	41
	$NiCl_2$	178
	$CoCl_2$	194
NaCl	$FeCl_3$	10
	$NiCl_2$	124
	$CoCl_2$	126

SUMMARY

1. A study of the crystallization of the salts NH_4Cl, NaCl, and KCl has demonstrated that the dendrites of these substances are single-crystal formations, growing from a single center.

2. The hypothesis is advanced that the production of dendritic forms is due to the combined action of two factors: a) the increased surface energy at the vertices and edges of crystals; this is the basic factor; the tendency to form dendrites is inherent in all three of the salts we have investigated, in different degree, depending upon the structure of their space lattices; and b) the uneven diffusion of the nutrient material into various elements of the crystal.

3. The action of admixtures of agar-agar and glycerol to the solution largely involves a diminution of the rate of diffusion and a promotion of the formation of dendrites.

4. Admixtures of Fe^{+++}, Ni^{++}, and Co^{++} ions retard the rate of growth at the vertices owing to their adsorption at the active centers of the crystal. This causes a marked change in the crystal habit: cubes settle out instead of dendritic forms.

5. The greater the tendency of a given substance to produce dendritic forms, the higher the boundary concentration of impurity ions in the solution required to break down the dendritic forms and convert them into the cubic form.

$$C_{\text{boundary}} \text{ for } NH_4Cl > C_{\text{boundary}} \text{ for } KCl > C_{\text{boundary}} \text{ for } NaCl.$$

6. We can arrange the tested impurity ions in order of decreasing effect upon the external form of crystals as follows: $Fe^{+++} > Ni^{++} > Co^{++}$.

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Received May 12, 1950.

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THE FUSIBILITY OF THE TERNARY SYSTEM: LEAD MONOXIDE — VANADIUM PENTOXIDE — TITANIUM DIOXIDE

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Titanium dioxide has been widely employed as a raw material for manufacturing ceramic condenser materials for the high-frequency radio industry because of its high dielectric susceptibility (> 100). Its high caking temperature and the large negative temperature coefficient of dielectric susceptibility (the temperature coefficient of capacitance ~-7 to $-9 \cdot 10^{-4}$) make it impossible to employ titanium dioxide in the pure state. To secure ceramic pastes with a temperature coefficient of capacitance close to zero fillers are added to titanium dioxide, but this, as a rule, greatly lowers the dielectric susceptibility as well (from 100 down to 15) [1]. The condenser pastes based on titanium dioxide manufactured at the present time that have a temperature coefficient of capacitance approaching zero all have a dielectric susceptibility that does not exceed 15 (with the sole exception of the tetrabar paste [2]).

It is therefore readily understood that we were greatly interested, from both the practical and the theoretical points of view, in discovering new fillers for titanium dioxide that would lower the temperature coefficient of capacitance of the ceramic pastes to values approaching zero while retaining the high values of dielectric susceptibility.

In our search for such fillers we have produced in our laboratory experimental samples containing lead vanadates that exhibit high values of electric susceptibility (50-70) and temperature coefficients of capacitance ranging from $-7 \cdot 10^{-4}$ to $+16 \cdot 10^{-4}$.

We have made a partial investigation of the fusibility of the ternary system $PbO-V_2O_5-TiO_2$ in order to ascertain the nature of the reaction of titanium dioxide with lead vanadates.

We employed the visual polythermal method in our research. A mixture of PbO, V_2O_5, and TiO_2 was placed in a platinum furnace and melted in a resistance furnace wound with Kornilov alloy, the temperature being measured by a Pt—Pt-Rh thermocouple that had been calibrated against: chemically pure KNO_3 — m.p. 337°, the $KCl-Na_2SO_4$ eutectic — m.p. 517°, KCl — m.p. 774°, Na_2SO_4 — m.p. 884°, and K_2SO_4 — m.p. 1069°.

The reagents used were as follows: titanium dioxide — prepared from titanic acid containing 99.5% TiO_2 and 0.5% CaO. The lead monoxide was prepared from the carbonate, produced by precipitation from chemically pure lead nitrate. The V_2O_5 was prepared from commercial ammonium vanadate.

We investigated the $PbO-TiO_2$ and $V_2O_5-TiO_2$ sides, repeated the previous investigation [3] of the $PbO-V_2O_5$ side, and 11 internal sections. The experimental data are set forth in Tables 1-11 and in Figs. 1 and 2.

The $PbO-TiO_2$ side was investigated up to 25 mol.% of TiO_2 (Table 1, Figure 1). The liquidus exhibits one eutectic point at 7.5 mol.% of TiO_2 and 818° and one transition point at 19 mol. % of TiO_2 and 1024°. The mixture consisting of 25 mol. % TiO_2 and 75 mol. % PbO melts at 1120°. At higher percentages of TiO_2 in the mixture, the TiO_2 does not dissolve while appreciable amounts of the PbO are volatilized, indicating decomposition of the compound that crystallizes after the transition point at 818°. The system thus exhibits two incongruently fusing compounds.

The $PbO-V_2O_5$ side had been investigated by Amadori previously [3]. We confirmed the existence of the congruently fusing compounds $8PbO \cdot V_2O_5$, $3PbO \cdot V_2O_5$, and $2PbO \cdot V_2O_5$. No metavanadate is found on the liquidus, the melt forming a glass in that region.

TABLE 1

Fusibility of the PbO – TiO_2 System

No.	Mol. % TiO_2	Temperature at which crystallization set in
1	0.0	884°
2	5.0	839
3	10.0	880
4	15.0	965
5	20.0	1030
6	25.0	1099
7	30.0	Did not fuse
8	35.0	Did not fuse

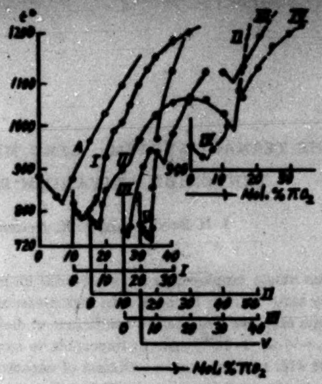

Fig. 1. Fusibility curves of the PbO – TiO_2 system (A) and of its sections:

I – $\left.\begin{matrix}5 \text{ mol.\% } V_2O_5\\95 \text{ mol.\% PbO}\end{matrix}\right\}$ + TiO_2 ;

II – $\left.\begin{matrix}11.1 \text{ mol.\% } V_2O_5\\88.9 \text{ mol.\% PbO}\end{matrix}\right\}$ + TiO_2;

III – $\left.\begin{matrix}16 \text{ mol.\% } V_2O_5\\84 \text{ mol.\% PbO}\end{matrix}\right\}$ + TiO_2;

IV – $\left.\begin{matrix}25 \text{ mol. \% } V_2O_5\\75 \text{ mol.\% PbO}\end{matrix}\right\}$ + TiO_2;

V – $\left.\begin{matrix}33.3 \text{ mol.\% } V_2O_5\\66.7 \text{ mol.\% PbO}\end{matrix}\right\}$ + TiO_2.

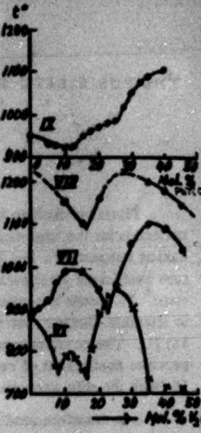

Fig. 2. Fusibility along the sections:

VI – $\left.\begin{matrix}2 \text{ mol.\% } TiO_2\\98 \text{ mol.\% PbO}\end{matrix}\right\}$ + V_2O_5;

VII – $\left.\begin{matrix}10 \text{ mol.\% } TiO_2\\90 \text{ mol.\% PbO}\end{matrix}\right\}$ + V_2O_5;

VIII – $\left.\begin{matrix}25 \text{ mol.\% } TiO_2\\75 \text{ mol.\% PbO}\end{matrix}\right\}$ + V_2O_5;

IX – $\left.\begin{matrix}25 \text{ mol .\% } V_2O_5\\75 \text{ mol.\% PbO}\end{matrix}\right\}$ + $PbTiO_3$;

The TiO_2 – V_2O_5 (the third side of the triangle) displays an infinitesimally small mutual solubility.

Section I: $\left.\begin{matrix}5 \text{ mol.\% } V_2O_5\\95 \text{ mol.\% PbO}\end{matrix}\right\}$ + TiO_2.

We managed to investigate the fusibility along this section up to 35 mol.% TiO_2. Five separate crystallization phases were found along this portion of the section: PbO crystallizes up to 2 mol.% TiO_2, then there comes a transition point at 780°, which is probably followed by the crystallization of the orthotitanate as minute round crystals. A phase not found on the side of the triangle crystallizes as the most minute dust in the interval between 5.5 mol.% TiO_2 (815°) and 8 mol.% TiO_2 (850°), while the orthotitanate again crystallizes from this phase up to 16 mol.% TiO_2 (1018°). Beyond the transition point (1018°) the compound $PbTiO_3$ crystallizes as large tetrahedral crystals. This phase continues to crystallize up to 35 mol.% TiO_2 and 1220°. Adding more titanium dioxide causes minute needles of titantium dioxide to settle out of the melt.

Section II: $\left.\begin{matrix}11.1 \text{ mol.\% } V_2O_5\\88.9 \text{ mol.\% PbO}\end{matrix}\right\}$ + TiO_2. This section has been investigated up to 45 mol.% TiO_2. As we follow the liquidus, the crystallization of $8PbO \cdot V_2O_5$ (from 3 mol.% TiO_2 and 765° to 14.5 mol.% TiO_2 and 918°) is followed by the crystallization of the phase consisting of minute dust, the orthotitanate phase observed along Section I being missing, a compound crystallizing as large (larger than 1 mm) four-sided platelets immediately after 14.5 mol.% TiO_2. Along this section the crystallization branch of this compound (the metatitanate $PbTiO_3$) exhibits a distinct maximum at 1170°. The point of joint crystallization of $PbTiO_3$ and TiO_2 occurs at 40 mol.% TiO_2 and 420°, after which titanium dioxide crystallized as thin, rather large needles.

Section III: $\left.\begin{matrix}16 \text{ mol. \% } V_2O_5\\84 \text{ mol.\% PbO}\end{matrix}\right\}$ + TiO_2. This section was investigated up to 41.5 mol.% TiO_2. In addition to the crystallization branch for $3PbO \cdot V_2O_5$, the liquidus distinctly shows other crystallization branches: a phase that crystallizes as dust (Sections I and II) and the metatitanate. Both branches exhibit distinct maxima (Fig. 1).

Section IV: $\left.\begin{matrix}25 \text{ mol. \% } V_2O_5\\75 \text{ mol. \%PbO}\end{matrix}\right\}$ + TiO_2. This section was investigated up to 33.3 mol. % TiO_2. The liquidus exhibits, in addition to the crystallization branch of $3PbO \cdot V_2O_5$, a short stretch of a phase consisting of fine dust (cf. Sections I, II, and III) and crystals of TiO_2. No metatitanate phase is found.

TABLE 2

Fusibility of the $PbO - V_2O_5$ System

No.	Mol. % V_2O_5	Temp. at which crystallization set in	Remarks
1	0.0	884*	
2	1.6	872	
3	3.5	855	
4	5.1	815	
5	6.0	793	
6	7.7	765	
7	10·0	765	Different phase
8	12.5	793	
9	15.2	748	
10	18.2	781	Different phase
11	21.4	884	
12	23.2	924	
13	25.0	952	
14	26.9	933	
15	29.0	851	
16	33.3	772	
17	38.2	692	
18	43.5	607	Different phase
19	50.0	497	Glass
20	57.2	518	Glass
21	65.4	582	Glass
22	75.0	651	Glass
23	86.4	666	Glass
24	100	675	Glass

TABLE 4

Section II: $\left.\begin{array}{r}11.1 \text{ mol. } \% \ V_2O_5 \\ 88.9 \text{ mol. } \% \ PbO\end{array}\right\} + TiO_2$

No.	Mol. % TiO_2	Temp. at which crystallization set in	Remarks
1	0.0	788	
2	1.0	777	
3	2.0	772	
4	3.0	777	
5	4.0	820	Different phase
6	5.0	850	
7	10.0	900	
8	15.0	970	
9	20.0	1128	Different phase
10	25.0	1154	
11	30.0	1168	
12	35.0	1160	
13	40.0	1128	Different phase
14	45.0	1184	
15	50.0	Did not fuse	
16	55.0	Did not fuse	

TABLE 3

Section I: $\left.\begin{array}{r}5 \text{ mol. } \% \ V_2O_5 \\ 95 \text{ mol. } \% \ PbO\end{array}\right\} + TiO_2$

No.	Mol. % TiO_2	Temp. at which crystallization set in	Remarks
1	0.0	820	
2	1.0	798	
3	3.0	788	
4	4.0	798	Different phase
5	5.0	809	
6	6.0	820	Different phase
7	7.0	835	
8	10·0	929	
9	12.5	988	
10	15.0	1011	
11	17.5	1053	Different phase
12	20.0	1096	
13	22.5	1135	
14	25.0	1160	
15	30.0	1198	
16	35.0	1220	
17	40.0	Did not fuse	
18	45.0	Did not fuse	

TABLE 5

Section III: $\left.\begin{array}{r}16 \text{ mol. } \% \ V_2O_5 \\ 84 \text{ mol. } \% \ PbO\end{array}\right\} + TiO_2$

No.	Mol. % TiO_2	Temp. at which crystallization set in	Remarks
1	0.0	757	
2	2.0	767	Different phase
3	4.0	830	
4	6.0	906	
5	8.0	946	
6	10.0	940	
7	15.0	981	Different phase
8	20.0	1065	
9	25.0	1128	
10	30.0	1128	
11	36.1	1135	Different phase
12	41.5	1190	
13	47.1	Did not fuse	

Section V: $\left.\begin{array}{l}33.3\text{ mol. \% }V_2O_5\\ 66.7\text{ mol. \% }PbO\end{array}\right\}+TiO_2$. We were able to trace this section only up to 10 mol. % TiO_2. The liquidus exhibits a single transition point (at 3 mol. % TiO_2 and 734°), the point of joint crystallization of $3PbO \cdot V_2O_5$ and TiO_2 (Figure 1).

Section VI. $\left.\begin{array}{l}2\text{ mol. \% }TiO_2\\ 98\text{ mol. \% }PbO\end{array}\right\}+V_2O_5$. The following features are displayed by the liquidus: a crystallization branch for PbO, which crystallizes as large, dark-brown platelets (up to 7 mol. % V_2O_5 and 750°), a crystallization branch for $8PbO \cdot V_2O_5$, which crystallizes as square, dark-brown crystals (up to 16 mol. % V_2O_5 and 732°), and a crystallization branch for $3PbO \cdot V_2O_5$, which crystallizes as hexahedral crystals. No pyrovanadate is found. Mixtures that contain 25 mol. % or more of V_2O_5 solidify as glasses.

Section VII. $\left.\begin{array}{l}10\text{ mol. \% }TiO_2\\ 90\text{ mol.\% }PbO\end{array}\right\}+V_2O_5$. The following crystallization branches are displayed on the liquidus: lead orthotitanate (4.5 mol.% V_2O_5 and 910°), a compound that crystallizes as a dust (up to 21.5 mol.% V_2O_5 and 890°), the branch for this compound exhibiting a maximum at 994°, and a crystallization branch for titanium dioxide, which can be followed up to 45 mol.% vanadium pentoxide. Mixtures containing more than 45 mol.% V_2O_5 solidify as glasses. The crystallization branch for titanium dioxide exhibits a maximum at 1110° (Fig. 2).

Section VIII: $\left.\begin{array}{l}25\text{ mol.\% }TiO_2\\ 75\text{ mol.\% }PbO\end{array}\right\}+V_2O_5$. All the mixtures lying along this section have melting points above 1000°. Up to 16 mol.% V_2O_5, $PbTiO_3$ crystallizes as large tetrahedral crystals, while at 20 mol.% V_2O_5 titanium dioxide crystallizes as large needles. The mixture is infusible at 1200° at from 25 to 35 mol.% of vanadium pentoxide, though as the concentration of V_2O_5 is increased still higher, the melting point of the mixture drops until a hyaline phase is formed (at 45 mol.% V_2O_5).

Section X: $\left.\begin{array}{l}50\text{ mol.\% }V_2O_5\\ 50\text{ mol.\% }PbO\end{array}\right\}+PbTiO_3$.

Section XI: $\left.\begin{array}{l}70\text{ mol.\% }V_2O_5\\ 30\text{ mol.\% }PbO\end{array}\right\}+TiO_2$.

A distinctive feature of these sections is the extremely low mutual solubility. At low percentages of lead titanate and titanium dioxide a hyaline phase is formed, from which insoluble titanium dioxide crystallizes out (large needles). The mixture is infusible when the $PbTiO_3$ or the TiO_2 totals more than 25 mol.%.

The data on the fusibility along the sides and the sections are plotted in the triangular fusibility diagram (Figure 3). The areas of crystallization of the following compounds are very clearly evident in the fusibility diagram for the system: (I) PbO; (II) $8PbO \cdot V_2O_5$; (III) $3PbO \cdot V_2O_5$; (IV) Pb_2TiO_4; (V) $PbTiO_3$; (VI) an inner ternary compound, the composition of which may approximate $10PbO \cdot V_2O_5 \cdot TiO_2$; (VII) the crystallization area for titanium dioxide; and (VIII) the area for the hyaline phase.

As we see by the diagram, lead orthotitanate and metatitanate, which are hard to distinguish on the liquidus of the binary system $PbO-TiO_2$, become more distinct when the third component (V_2O_5) is added, possessing their own crystallization areas. The metatitanate ($PbTiO_3$) crystallizes very well as large (exceeding 1 mm) tetrahedral flakes (Sections I, II, and III). The area of crystallization of the metatitanate in the ternary system diagram defines the compositions that may be recommended for the growing of large crystals of lead metatitanate. These findings indicate that we must not start with the stoichiometric proportions of lead monoxide and titanium dioxide if we want to secure crystals of lead metatitanate, but must employ a large excess of lead monoxide (70-75 mol. % PbO and 25 mol. % TiO_2). Lead orthotitanate (Pb_2TiO_4) crystallizes as extremely minute crystals. It is hard to secure large crystals.

Some very satisfactory crystallization has been observed: that of lead monoxide as large brown crystals (Sections I and VI) and that of the compounds $8PbO \cdot V_2O_5$ and $3PbO \cdot V_2O_5$, likewise as large crystals (Sections II, III, and IV).

The absence of crystallization areas for the compounds $2PbO \cdot V_2O_5$ and $PbO \cdot V_2O_5$ is worthy of note. Mixtures consisting of lead monoxide and vanadium pentoxide in proportions corresponding to these compounds form hyaline masses in the presence of titanium dioxide, although the compounds do crystallize when no titanium dioxide is present. Titanium dioxide crystallizes as large needles (Sections I, X, and XI) from the hyaline phase (this region is outlined by a dotted line in Figure 3).

TABLE 6

Section IV: $\left.\begin{matrix}25\text{ mol. \% }V_2O_5\\75\text{ mol. \% }PbO\end{matrix}\right\} + TiO_2$

No.	Mol. % TiO_2	Temp. at which crystallization sets in	Remarks
1	0.0	956	
2	3.7	929	
3	6.7	942	Different phase
4	11.7	1000	
5	15.8	1064	Different phase
6	20.0	1132	
7	24.3	1180	
8	28.8	1213	
9	33.3	1232	
10	40.0	Did not fuse	

TABLE 7

Section V: $\left.\begin{matrix}33.3\text{ mol. \% }V_2O_5\\66.7\text{ mol. \% }PbO\end{matrix}\right\} + TiO_2$

No.	Mol. % TiO_2	Temp. at which crystallization sets in	Remarks
1	0.0	772	
2	0.5	767	
3	1.5	748	
4	2.3	742	
5	3.3	762	Different phase
6	4	857	
7	5	970	
8	10	1130	
9	15	Did not fuse	
10	20	Did not fuse	

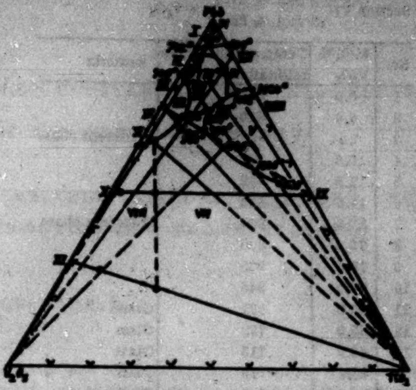

Fig. 3. Fusibility in the $PbO-V_2O_5-TiO_2$ Ternary System.

I) PbO; II) $8PbO \cdot V_2O_5$; III) $3PbO \cdot V_2O_5$; IV) $2PbO \cdot TiO_2$; V) $PbO \cdot TiO_2$; VI) $10PbO \cdot V_2O_5 \cdot TiO_2$; VII) TiO_2; VIII) hyaline phase.

The ternary compound (Figure 3, Area VI) fuses incongruently along Sections I, II, and IV, fusing congruently along Sections III and VII. The section data enabled us to establish its approximate composition as $10PbO \cdot V_2O_5 \cdot TiO_2$ and its melting point as approximately 1000°.

The crystallization area for titanium dioxide occupies more than half the triangle (Figure 3, Area VII). Titanium dioxide crystallizes as large needles in the regions adjacent to the crystallization areas for chemical compounds. These crystals look like those of rutile. The ternary system compositions in the regions adjacent to the crystallization areas for $PbTiO_3$, $10PbO \cdot V_2O_5 \cdot TiO_2$, and $3PbO \cdot V_2O_5$ and in the region of glass formation may be recommended for cultivating the large crystals of titanium dioxide required for research on their dielectric properties.

In conclusion, it must be stated that it is extremely difficult to make a fusibility investigation of this system because of the total opacity of the melts and the high melting point of titanium dioxide.

SUMMARY

1. A partial investigation has been made of the fusibility of the ternary system $PbO-V_2O_5-TiO_2$. The fusibility diagram of the ternary system exhibits the crystallization areas of PbO, Pb_2TiO_4, $PbTiO_3$, $8PbO \cdot V_2O_5$, $3PbO \cdot V_2O_5$, a compound produced for the first time with the approximate composition of $10PbO \cdot V_2O_5 \cdot TiO_2$, and titanium dioxide, as well as a region in which a glass is formed.

TABLE 8

Section VI: $\left.\begin{matrix}2\text{ mol. \% }TiO_2\\98\text{ mol. \% }PbO\end{matrix}\right\}+V_2O_5$

No.	Mol. % V_2O_5	Temp. at which crystallization sets in	Remarks
1	0.0	881*	
2	5.0	810	
3	7.5	760	Different phase
4	10.0	787	
5	12.5	782	
6	15.0	754	
7	17.5	804	Different phase
8	20.0	890	
9	22.5	935	
10	25.0	948	
11	30.0	901	Glass
12	35.0	732	Glass
13	40.0	716	Glass
14	45.0	710	Glass
15	50.0	682	Glass
16	55.0	644	Glass

TABLE 9

Section VII: $\left.\begin{matrix}10\text{ mol. \% }TiO_2\\90\text{ mol. \% }PbO\end{matrix}\right\}+V_2O_5$

No.	Mol. % V_2O_5	Temp. at which crystallization sets in	Remarks
1	0.0	878*	
2	2.5	901	
3	5.0	918	
4	7.5	964	Different phase
5	10.0	987	
6	15.0	987	
7	20.0	947	
8	25.0	958	Different phase
9	30.0	1052	
10	35.0	1102	
11	40.0	1090	
12	45.0	1040	
13	50.0	Glass	

TABLE 10

Section VIII: $\left.\begin{matrix}25\text{ mol. \% }TiO_2\\75\text{ mol. \% }PbO\end{matrix}\right\}+V_2O_5$

No.	Mol. % V_2O_5	Temp. at which crystallization sets in	Remarks
1	10.0	1056*	
2	15.0	1102	
3	20.0	1162	Different phase,
4	25.0	Did not fuse	
5	30.0	Did not fuse	
6	35.0	1200	
7	40.0	1182	
8	45.0	1150	
9	50.0	Glass	

TABLE 11

Section IX: $\left.\begin{matrix}25\text{ mol. \% }V_2O_5\\75\text{ mol. \% }PbO\end{matrix}\right\}+PbTiO_3$

No.	Mol. % $PbTiO_3$	Temp. at which crystallization sets in	Remarks
1	0.0	952*	
2	5.0	935	
3	7.3	930	
4	10.0	924	
5	12.5	924	Different phase
6	15.0	947	
7	17.5	961	
8	20.0	970	
9	22.5	981	
10	25.0	987	
11	27.5	1017	
12	30.0	1052	Different phase, hexahedra
13	32.5	1077	
14	35.0	1089	
15	40.0	1102	
16	45.0	1114	

2. It has been shown that two incongruently fusing compounds ($2PbO \cdot TiO_2$ and $PbO \cdot TiO_2$) are formed in the $PbO-TiO_2$ system. The presence of vanadium pentoxide increases the stability of the metatitanate.

3. The component concentrations that are most suitable for growing large crystals of lead metatitanate and titanium dioxide are outlined.

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Received April 24, 1950.

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ABSORPTION SPECTRA AND DISSOCIATION CONSTANTS OF DIPHENYLTHIOCARBAZONE (DITHIZONE) AND OF ITS INNER COMPLEX SALTS

I. ABSORPTION SPECTRA OF DIPHENYLTHIOCARBAZONE (DITHIZONE) AND ITS EQUILIBRIUM DISTRIBUTION IN A TWO-PHASE SYSTEM

R. E. Chernitskaya

The absorption spectra of many colored organic compounds exhibit a displacement of the maximum on the absorption curve and a change in the intensity of the absorption maximum with the properties of the solvent.

We have investigated the effect of the polar properties of the solvent upon the absorption spectrum of diphenylthiocarbazone (dithizone). As we know, dithizone produces highly colored solutions in organic solvents [1] and is a sensitive reagent for detecting traces of the heavy metals. The absorption curve of a solution of dithizone in carbon tetrachloride exhibits two maxima in the 620 mμ and 450 mμ regions; the absorption maximum of the dithizone ion is located in the 480-490 mμ region. We have secured the absorption spectra of dithizone in benzene, hexane, methyl ethyl ketone, and isoamyl alcohol.

The benzene bore the label "pure, for analysis"; the hexane we used was the fraction boiling in a two-degree interval (67-69°). The methyl ethyl ketone was refined via the bisulfite compound, from which it was isolated by distillation at 79-80°. The isoamyl alcohol was refined by treating it with 5% sulfuric acid to eliminate the pyridine and other organic bases and their homologs. The final product was collected at a boiling point of 128.5-129.5°.

The absorption spectra were secured with a Hilger photoelectric spectrometer for the visible region; they are shown in Fig. 1. The width of the absorption band did not exceed 29 A in the 5000 A region. The values of $\lambda_{1\max}$ and $\lambda_{2\max}$ we secured are listed in Table 1, together with the corresponding values of μ – the dipole moment.

TABLE 1

No.	Solvent	$\lambda_{1\max}$ (mμ)	$\lambda_{2\max}$ (mμ)	$\mu \cdot 10^{18}$ electrostatic units
1	Benzene..........	600	450	0
2	Hexane...........	600	435	0.05
3	Methyl ethyl ketone.........	590	460	2.79
4	Isoamyl alcohol	580	460	1.85
5	Carbon tetrachloride[2]	620	450	0

As we see in Table 1, the location of the two maxima depends upon the polar properties of the solvent. The wavelength of the first maximum ($\lambda_{1\max}$), for instance, is displaced toward the shorter wavelengths,

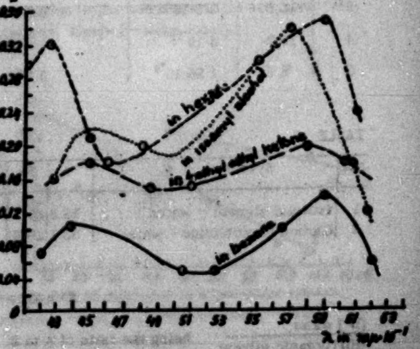

Fig. 1. Absorption spectra of dithizone in various solvents.

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[1] A.A.Pryanishnikov was good enough to communicate to me methods of purifying methyl ethyl ketone and isoamyl alcohol, for which I am deeply grateful.

[2] We have taken the values of $\lambda_{1\max}$ and $\lambda_{2\max}$ from the data in the literature.

while the wavelength of the second maximum ($\lambda_{2\,max}$) is shifted to the longer wavelengths as the polarity of the solvent increases. The position of the $\lambda_{1\,max}$ of dithizone dissolved in isoamyl alcohol exhibits the greatest shift, compared with its solution in an inert solvent.

We have measured and calculated the equilibrium distribution of dithizone in two phases in the isoamyl alcohol – water system, as was done in the paper by A. Babko and Pilipenko [1] for carbon tetrachloride – water.

The solutions of dithizone in isoamyl alcohol were prepared as follows: the initial dithizone was dissolved in isoamyl alcohol and treated with a 0.5% solution of ammonia, after which it was again isolated in isoamyl alcohol by reacting the ammonium salt of dithizone with a 5% solution of hydrochloric acid. The initial preparation of dithizone was obtained by decomposing the phenylthiocarbazonate with phenylhydrazine.

The equilibrium distribution of the dithizone in the 2-phase system was determined as follows: 5 ml of a solution of dithizone in isoamyl alcohol (concentration = $2.08 \cdot 10^{-3}$ moles per liter) was diluted with 10 ml of isoamyl alcohol, and then 15 ml of the appropriate buffer mixture (acetic acid + ammonia) was added. The mixture was agitated for 2 minutes and then allowed to stand for 10 minutes until the layers separated completely.

The optical density of the isoamyl alcohol layer was measured. The dithizone was extracted from the aqueous layer by adding acid and isoamyl alcohol and transferred to the isoamyl alcohol, the optical density of the dithizone extracted from the water being measured in the isoamyl alcohol.

We first plotted a calibration curve for the variation of optical density with the concentration of the dithizone in millimoles per liter. This was done at 20°. As we know from the findings of Kablukov and Malyshev [2], 2.9 ml of isoamyl alcohol dissolves in 100 ml of water at this temperature.

To allow for this we proceeded as follows: the isoamyl alcohol with which the mixture was diluted was allowed to stand for one hour with the appropriate buffer mixture (1/3 volume per volume of buffer mixture); on the other hand, a solution of dithizone in isoamyl alcohol was allowed to stand for an hour with water (1/3 volume per volume of the solution of dithizone in isoamyl alcohol).

We measured the optical density in a Hilger absorptiometer. The cell thickness was 10 mm, the light filter used was a No. 607. Our results are given in Table 2.

TABLE 2

No.	pH	[H]	Amount of dithizone in water, millimoles $\cdot 10^4$	Amount of dithizone in isoamyl alcohol, millimoles $\cdot 10^4$	A,%	B,%	K'_{HD}
1	10.6	$2.5 \cdot 10^{-11}$	0.128	0.395	31.5	68.4	$0.08 \cdot 10^{-10}$
2	11.0	$1 \cdot 10^{-11}$	0.224	0.317	41.0	58.6	$0.05 \cdot 10^{-10}$
3 1)	10.6	$2.5 \cdot 10^{-11}$	0.545	1.09	33	66	$0.08 \cdot 10^{-10}$
4	10.2	$3 \cdot 10^{-11}$	0.545	1.172	31.8	68.2	$0.2 \cdot 10^{-10}$
5	8.9	$1.26 \cdot 10^{-9}$	0.273	1.104	19.8	80.1	$2.0 \cdot 10^{-10}$

TABLE 3

No.	System	A	B	$\lambda_{1\,max}$	$\lambda_{2\,max}$
1	Isoamyl alcohol – water........	19.8	80.1	1450	620
2	Carbon tetrachloride – water	83.1	16.9	30400 [3]	1900 [3]

The values of K'_{HD} given in column 8 were calculated as shown in the paper by A. Babko and Pilipenko, based on the concepts of the dissociation of dithizone as a monobasic acid. The dissociation constant (K') of dithizone is defined as follows:

$$K' = K_p = \frac{[H^+][D^-]\ \text{water}}{[HD]\ \text{organic solvent}}$$

$\frac{[D^-]\ \text{water}}{[HD]\ \text{organic solvent}}$ being the ratio of A to B, as measured by us for various values of pH.

The values of A and B determined by us for pH = 8.8 were compared with the corresponding values obtained for these quantities by A. Babko and Pilipenko for the carbon tetrachloride – water system at pH = 8.9.

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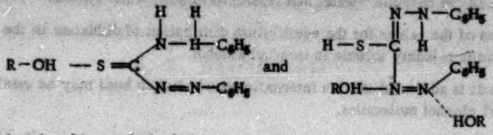
1) See following page.

At the same time we compared the intensity of the absorption maxima for the dithizone solutions in the two systems. Our results are given in Table 3.

As we see in Table 3, the weakening in the intensity of both maxima on the spectral curves for the solution of dithizone in isoamyl alcohol corresponds approximately to the change in the distribution of dithizone between the two phases in the isoamyl alcohol – water system, as contrasted with the carbon tetrachloride – water system.

These findings led us to assume an increased solubility of dithizone in isoamyl alcohol and that an intermolecular hydrogen bond might be established between the molecules of dithizone and isoamyl alcohol as follows:



where R—OH is a molecule of isoamyl alcohol.

Compounds of this sort are much less soluble, of course, in alkalis, owing to possible steric hindrances. The substantial drop of the value of λ_{max} (from 620 to 580 mμ) in isoamyl alcohol is further evidence of interaction between the dithizone and isoamyl alcohol molecules.

We also determined the equilibrium distribution of dithizone in a benzene – water solution. These measurements were made with a Hilger absorptiometer with a cell 10 mm thick. The light filter used was a No. 607. The concentration of the initial solution was $2.604 \cdot 10^{-4}$ moles/liter. Our findings are given in Table 4.

TABLE 4

No.	pH	[H]	Amount of dithizone in water, millimoles $\cdot 10^3$	Amount of dithizone in benzene, millimoles $\cdot 10^3$	A,%	B,%	K^*_{HD}
1	7.35	$4.46 \cdot 10^{-8}$	0.0325	0.8854	3.54	90	$1.73 \cdot 10^{-9}$
2	8.9	$1.96 \cdot 10^{-9}$	0.4036	0.5534	42.2	57.8	$0.36 \cdot 10^{-9}$
3	10.2	$6.3 \cdot 10^{-11}$	0.8333	0.1303	86.46	13.5	$0.31 \cdot 10^{-9}$
4	10.6	$2.5 \cdot 10^{-11}$	0.8884	0.7181	91.9	8.1	$0.22 \cdot 10^{-9}$
							$0.29 \cdot 10^{-9}$ [2]

We then compared our findings for the equilibrium distribution in the benzene – water and isoamyl alcohol – water systems (with the reservations made for the isoamyl alcohol – water case.).

The distribution data are shown in Figure 2. Inspection of these curves indicates that the equilibrium distribution at various values of pH in the benzene – water system approaches the distribution secured by A. Babko and Pilipenko for the carbon tetrachloride – water system; as for the isoamyl alcohol – water system, its curve is flatter, being nearly parallel to the axis of abscissas at pH 11.

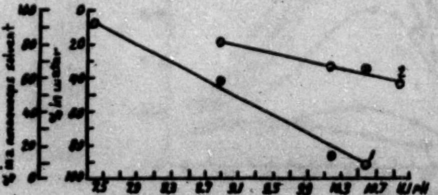


Fig. 2. Distribution of dithizone in a two-phase system.
1) Benzene – water; 2) isoamyl alcohol – water.

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[1] The concentration of the dithizone solution was $2.09 \cdot 10^{-3}$ millimoles per liter in Tests 3, 4, and 5. We have expressed the amounts of dithizone found in the two phases in the dithizone concentration in millimoles, corresponding to the values of optical density. The values of A and B are given in per cent distribution in the two phases.

[2] We used the average of the last three determinations as our mean value. In this case, as in the case of isoamyl alcohol, we were more interested in the order of magnitude of K^* and in the possibility of comparing the values of A and B for the same pH values than in the absolute value of these quantities. This is why we felt we could be satisfied with a few determinations.

Moreover, the values we have found for K'_{HD} for solutions of dithizone in isoamyl alcohol and in benzene bear out the hypothesis advanced above that dithizone is a monobasic acid.

SUMMARY

1. An equation has been found that expresses the variation of the position and intensity of the maxima on the curve of spectral absorption for dithizone solutions with the polar properties of the solvent.

2. The equilibrium distribution of dithizone in the isoamyl alcohol – water and the benzene – water system has been measured and calculated. The K'_{HD} has been calculated by the A.Babko and Pilipenko method for solutions of dithizone in the benzene – water and isoamyl alcohol – water systems.

3. A comparison of the values for the equilibrium distribution of dithizone in the two systems led to the conclusion that dithizone is highly soluble in isoamyl alcohol.

4. The hypothesis is advanced that an intermolecular hydrogen bond may be established between the dithizone and isoamyl alcohol molecules.

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Received May 8, 1950.

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THE ABSORPTION SPECTRA AND DISSOCIATION CONSTANTS OF DIPHENYLTHIOCARBAZONE (DITHIZONE) AND OF ITS INNER COMPLEX SALTS

II. ABSORPTION SPECTRA AND INSTABILITY CONSTANTS OF INNER COMPLEX SALTS OF DITHIZONE DISSOLVED IN ISOAMYL ALCOHOL

R. E. Chernitskaya

In our previous paper [1] research on the curve of spectral absorption of dithizone dissolved in isoamyl alcohol and determinations of the equilibrium distribution of dithizone in the isoamyl alcohol—water system served as a basis for our presupposing that dithizone molecules react with molecules of isoamyl alcohol, establishing an intermolecular hydrogen bond between them.

In the present paper we have determined the absorption spectra and instability constants of various inner complex salts of dithizone produced in an isoamyl alcohol solution.[1]

We have secured the absorption spectra of the inner salts of silver, mercury, copper, zinc, lead, cadmium, and bismuth with the Hilger photoelectric spectrometer (for the visible region). The inner complex salts were prepared as follows: 3 ml of a solution of dithizone in isoamyl alcohol was added to 1.5 ml of a solution of the salt of the respective metallic cation, 1.5 ml of the dithizone solution being used in the case of silver. The mixture was shaken in a separatory funnel for 2 minutes, and then it was allowed to stand for 10 minutes to separate the layers completely. The cell used was 10 mm thick. Isoamyl alcohol served as the control liquid. The concentrations of the salt solutions and of the dithizone solution were 10^{-4} mole per liter.

The absorption spectra of the dithizonates are shown in the figure.

The values of λ_{max} of the absorption curves of the inner complex salts of dithizone are given in Table 1.

TABLE 1

No.	Dithizone, inner complex salt of	λ_{max} in isoamyl alcohol (mμ)	λ_{max} in CCl_4 (mμ)	$\Delta\lambda_{max}$ in isoamyl alcohol (mμ)	$\Delta\lambda_{max}$ in CCl_4 (mμ)
1	Silver	450	460	130	160
2	Zinc	505	535	75	85
3	Cadmium . . .	500	510	80	110
4	Mercury	490	530	90	90
5	Lead	505	525	75	95
6	Copper	500	510	80	110
7	Bismuth	495	500	85	120

The λ_{max} of the absorption spectrum of dithizone in isoamyl alcohol is 580 mμ. The λ_{max} of the absorption spectrum of dithizone dissolved in CCl_4 is 620 mμ.

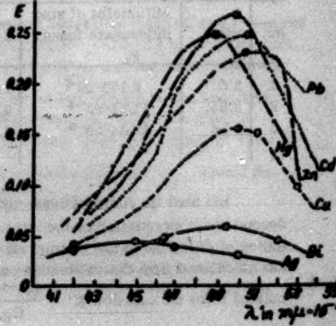

Figure. Absorption spectra of dithizonates.

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[1] The laboratory assistant V. G. Tararashkina participated in this research

The data listed in Table 1 indicate that the shift of the λ_{max} (toward the ultra-violet) of the inner complex salt of dithizone in isoamyl alcohol with respect to the λ_{max} of the solution of pure dithizone ($\Delta\lambda_{max}$) in isoamyl alcohol is less than in the carbon tetrachloride solution.

We have determined the instability constants of the inner complex salts of silver, copper, zinc, lead, and cadmium dithizonates, prepared in isoamyl alcohol.

We measured the instability constants by the method described in the papers of A. Babko and Pilipenko [2,3], using a Hilger absorptiometer with the appropriate light filters. The cell was 10 mm thick. Isoamyl alcohol was used as the control liquid.

The concentrations of the dithizone solution in isoamyl alcohol and of the original metal salt were about 10^{-4} mole per liter.

Our findings are set forth in Tables 2-7.

TABLE 2

Instability Constant of Silver Dithizonate Dissolved in Isoamyl Alcohol

Initial concentrations: Ag^+ in water: $9.27\cdot10^{-4}$ mole/liter; dithizone in isoamyl alcohol: $8.59\cdot10^{-4}$ mole/liter

No.	pH	Millimoles of silver dithizonate found, P_0	Equilibrium concentrations, moles/liter			K'_{AgD}
			Ag^+ in water	$C_{MC}\cdot10^4$ in isoamyl alcohol	$C_{KC}\cdot10^4$ in isoamyl alcohol	
1	5.16	$0.74\cdot10^{-4}$	$9.205\cdot10^{-4}$	8.096	0.247	$0.18\cdot10^{-9}$
2	5.19	$1.25\cdot10^{-4}$	$9.161\cdot10^{-4}$	7.76	0.417	$0.09\cdot10^{-9}$
3	5.22	$0.71\cdot10^{-4}$	$9.208\cdot10^{-4}$	8.12	0.233	$0.17\cdot10^{-9}$
4	5.06	$1.4\cdot10^{-4}$	$9.148\cdot10^{-4}$	7.66	0.466	$0.12\cdot10^{-9}$
5	5.16	$4.63\cdot10^{-4}$	$9.229\cdot10^{-4}$	8.28	0.154	$0.31\cdot10^{-9}$
6	5.36	$4.63\cdot10^{-4}$	$9.228\cdot10^{-4}$	8.28	0.154	$0.19\cdot10^{-9}$
7	4.88	$1.09\cdot10^{-4}$	$9.175\cdot10^{-4}$	7.86	0.363	$0.23\cdot10^{-9}$
8	5.48	$1.06\cdot10^{-4}$	$9.177\cdot10^{-4}$	7.88	0.354	$0.06\cdot10^{-9}$
9	5.48	$0.7\cdot10^{-4}$	$9.209\cdot10^{-4}$	8.12	0.233	$0.01\cdot10^{-9}$
				Average		$0.15\cdot10^{-9}$

TABLE 3

Instability Constant of Zinc Dithizonate Dissolved in Isoamyl Alcohol.

Initial concentrations: Zn^{++} in water: $1.871\cdot10^{-3}$ mole/liter; dithizone in isoamyl alcohol: $2.24\cdot10^{-4}$ mole/liter

No.	pH	Millimoles of zinc dithizonate found, P_0	Equilibrium concentrations, moles liter			K'_{ZnD_2}
			Zn^{++} in water	$C_{MC}\cdot10^4$ in isoamyl alcohol	$C_{KC}\cdot10^4$ in isoamyl alcohol	
1	3.6	$6.173\cdot10^{-5}$	$1.135\cdot10^{-3}$	1.82846	0.20576	$0.29\cdot10^{-22}$
2	3.85	$11.11\cdot10^{-5}$	$0.905\cdot10^{-5}$	1.499	0.3703	$0.28\cdot10^{-22}$
3	4.56	$12.44\cdot10^{-5}$	$0.789\cdot10^{-5}$	1.4106	0.4146	$0.9\cdot10^{-22}$
				Average		$0.49\cdot10^{-22}$

We used the computational method and the notation given in the paper by A.Babko and Pilipenko: C_{KC} denotes the concentration of the inner complex dithizone salt in the isoamyl alcohol phase; C_{MC} the concentration of dithizone in the isoamyl alcohol; P_0 the amount of the inner complex salt, expressed in millimoles and calculated from the calibration curve (optical density vs. millimoles of the dithizonate); and K' was calculated from the equation $K' = \frac{Me^{++}[D']^2}{C_{KC}}$, where Me^{++} is the equilibrium concentration of the cation of the given metal in water, D' is the concentration of the anion of the dithizone molecule, which we had previously found [1] from the equation $K'_{HD} = \frac{[H][D']}{[HD]}$.

TABLE 4

Instability Constant of Cadmium Dithizonate Dissolved in Isoamyl Alcohol.

Initial concentrations: Cd^{++} in water: $2.965 \cdot 10^{-5}$ mole/liter; dithizone in isoamyl alcohol: $3.125 \cdot 10^{-4}$ mole/liter.

No.	pH	Millimoles of cadmium dithizonate found, P_0	Equilibrium concentrations, moles/liter			K'_{CdD_2}
			Cd^{++} in water	$C_{MC} \cdot 10^4$ in isoamyl alcohol	$C_{KC} \cdot 10^4$ in isoamyl alcohol	
1	3.6	$1.335 \cdot 10^{-4}$	$1.804 \cdot 10^{-5}$	2.235	0.445	$0,32 \cdot 10^{-22}$
2	4.18	$2,468 \cdot 10^{-4}$	$1.688 \cdot 10^{-5}$	2.087	0.489	$0,36 \cdot 10^{-22}$
3	3.2	$0,7563 \cdot 10^{-4}$	$2,307 \cdot 10^{-5}$	2,621	0,2521	$0,41 \cdot 10^{-22}$
4	3,06	$1,2267 \cdot 10^{-4}$	$2,769 \cdot 10^{-5}$	2,974	0.0756	$0,43 \cdot 10^{-22}$
				Average		$0,38 \cdot 10^{-22}$

TABLE 5

Instability Constant of Mercury Dithizonate Dissolved in Isoamyl Alcohol.

Initial concentrations: Hg^{++} in water: $4.98 \cdot 10^{-4}$ mole/liter; dithizone in isoamyl alcohol: $6.25 \cdot 10^{-4}$ mole/liter.[1)]

No.	pH	Millimoles of mercury dithizonate found, P_0	Equilibrium concentrations, moles/liter			K'_{HgD_2}
			Hg^{++} in water	$C_{MC} \cdot 10^4$ in isoamyl alcohol	$C_{KC} \cdot 10^4$ in isoamyl alcohol	
1	4,93	$2.49 \cdot 10^{-4}$	$4.763 \cdot 10^{-4}$	4.59	0.83	$0.71 \cdot 10^{-18}$
2	4.89	$3.16 \cdot 10^{-4}$	$4.531 \cdot 10^{-4}$	2.81	1.72	$0,1 \cdot 10^{-18}$
3	4.79	$3.69 \cdot 10^{-4}$	$4,659 \cdot 10^{-4}$	3.79	1.23	$0,16 \cdot 10^{-18}$
4	4.6	$2.49 \cdot 10^{-4}$	$4,769 \cdot 10^{-4}$	4.59	0.83	$0,16 \cdot 10^{-18}$
5	4.5	$4.2 \cdot 10^{-4}$	$4,614 \cdot 10^{-4}$	3.45	1.4	$0,03 \cdot 10^{-18}$
6	4,93	$4.492 \cdot 10^{-4}$	$4.768 \cdot 10^{-4}$	3,34	0.83	$0,37 \cdot 10^{-18}$
7	4.86	$1.236 \cdot 10^{-4}$	$4.876 \cdot 10^{-4}$	4.2	0.42	$0,87 \cdot 10^{-18}$
				Average		$0,39 \cdot 10^{-18}$

Notes to Tables 2-5: 1) The volume of the aqueous phase was 11.5 ml in all the tests.
2) The volume of the nonaqueous phase was 3 ml in all the tests.

The values we found for the constant $K' = KP$, where K was the true instability constant, and P was the distribution coefficient of the inner complex salt in the two phases. By taking the value of P to be approximately the same for any given solvent, we were able, however, to compare the K' as true instability constants.

We made a comparison of the values of the instability constant K' we had secured for the specified inner complex salts of dithizone with the values of λ_{max} listed in Table 1 above and with the values of $\varepsilon\lambda_{max}$ that we had calculated for the respective inner complex salts. These findings are listed in Table 8.

Table 8 indicates that as the complex salt's instability constant rises, the shift of λ_{max} toward the ultraviolet region is increased, while the intensity of λ_{max} diminishes.

We endeavored to determine the composition of the silver dithizonate complex salt dissolved in isoamyl alcohol by the Job method. We equipped an ISP-51 spectrograph to measure absorption spectra: the light source was a 100-watt bulb with a straight wolfram filament, which yielded a continuous spectrum in the visible region, the measurement cell being a brass tube (Bailey) gilded on the inside, with a screw thread that made it possible to read the layer thicknesses to 0.01 mm.

The wavelength standard was the spectrum of the iron arc. Isoortho photographic plates with a speed of 400 HD were used.

[1)] The initial concentrations in Tests 6 and 7 were as follows: Hg^{++} in water: $4.985 \cdot 10^{-4}$ mole/liter; and dithizone in isoamyl alcohol: $5.039 \cdot 10^{-4}$ mole/liter.

TABLE 6

Instability Constant of Lead Dithizonate Dissolved in Isoamyl Alcohol

Initial concentrations: Pb^{++} in water – $9 \cdot 10^{-4}$ mole/liter; dithizone in isoamyl alcohol: $3.8 \cdot 10^{-4}$ mole/liter.

No.	pH	Millimoles of lead dithizonate found, P_s	Equilibrium concentration, mole/liter			K'_{PbD_2}
			Pb^{++} in water	$C_{MC} \cdot 10^4$ in isoamyl alcohol	$C_{KC} \cdot 10^4$ in isoamyl alcohol	
1	3.01	$2.896 \cdot 10^{-4}$	$8.75 \cdot 10^{-4}$	6.069	0.9653	$0.35 \cdot 10^{-21}$
2	3.21	$4.967 \cdot 10^{-4}$	$8.57 \cdot 10^{-4}$	4.689	1.6556	$0.3 \cdot 10^{-21}$
3	3.8	$9.653 \cdot 10^{-4}$	$8.16 \cdot 10^{-4}$	1.565	3.2176	$0.317 \cdot 10^{-21}$
4	2.98	$1.931 \cdot 10^{-4}$	$8.83 \cdot 10^{-4}$	6.712	0.6433	$0.56 \cdot 10^{-21}$
				Average.......		$0.38 \cdot 10^{-21}$

TABLE 7

Instability Constant of Copper Dithizonate Dissolved in Isoamyl Alcohol

Initial concentrations: Cu^{++} in water: $1.58 \cdot 10^{-4}$ mole/liter; dithizone in isoamyl alcohol: $8.594 \cdot 10^{-4}$ mole/liter

No.	pH	Millimoles of copper dithizonate found, P_s	Equilibrium concentration, moles per liter			K'_{CuD_2}
			Cu^{++} in water	$C_{MC} \cdot 10^4$ in isoamyl alcohol	$C_{KC} \cdot 10^4$ in isoamyl alcohol	
1	4.13	$2.523 \cdot 10^{-4}$	$1.361 \cdot 10^{-4}$	6.912	0.841	$1.6 \cdot 10^{-20}$
2	4.0	$2.203 \cdot 10^{-4}$	$1.388 \cdot 10^{-4}$	7.126	0.734	$1.23 \cdot 10^{-20}$
3	3.85	$4.963 \cdot 10^{-4}$	$1.236 \cdot 10^{-4}$	5.954	1.32	$0.13 \cdot 10^{-20}$
4	3.6	$3.487 \cdot 10^{-4}$	$1.276 \cdot 10^{-4}$	6.269	1.162	$0.55 \cdot 10^{-20}$
5	3.4	$2.305 \cdot 10^{-4}$	$1.379 \cdot 10^{-4}$	7.057	0.768	$0.46 \cdot 10^{-20}$
				Average........		$0\ 71 \cdot 10^{-20}$

TABLE 8

No.	Inner complex, dithizone salt of	K'	λ_{max} (mμ)	$\varepsilon\lambda_{max}$
1	Silver	$0.15 \cdot 10^{-7}$	450	110
2	Mercury	$0.39 \cdot 10^{-18}$	490	700
3	Zinc	$0.49 \cdot 10^{-22}$	505	600
4	Lead	$3.8 \cdot 10^{-22}$	505	710
5	Copper	$0.71 \cdot 10^{-20}$	500	600
6	Cadmium	$0.38 \cdot 10^{-22}$	510	800

The blackening marks were produced by means of a step-by-step platinum clearing agent.

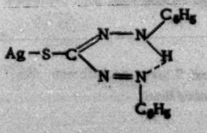
The absorption spectra were photographed through a solution of the inner complex salt silver dithizonate, the ratios between the ml of the initial silver salt solution and the solution of dithizone in isoamyl alcohol being as follows (both solutions having the same concentration: 10^{-4} mole per liter).

Ml of the silver salt solution	Ml of the dithizone solution
0.5	2.5
1.5	1.5
2	1.0
2.5	0.5

The blackening marks were photographed on the same plate as the silver dithizonate solutions. The solution pH was 6.8. After the photometric readings had been taken with a MF-2 microphotometer, the degree of blackening of the plate was evaluated at two points in the spectrum: 560 mμ and 460 mμ. We used a somewhat simplified method of estimating the degree of blackening, this simplification consisting in estimating the degree of blackening at the point of absorption via the points of equal blackening for the control liquid as photographed with the step-by-step clearing agent and for the test spectrum, instead of plotting a blackening curve for the given wavelength.

Taking photometric readings of a large number of photographic plates bearing the spectra of the inner complex silver salt, photographed at the ratios indicated above we found that the difference in intensity of blackening was a maximum at 580 mμ (the λ_{max} for pure dithizone) and at 460 mμ (the λ_{max} for silver dithizonate) at a 1:1 molar ratio of the silver salt solution for the dithizone solution.

These findings led us to this formula for silver dithizonate: AgD (where D is the dithizonate ion) from which it follows that the structure of silver dithizonate may be as follows:



The intramolecular hydrogen bond within the dithizone ion itself, together with the possible interaction of the dithizone molecule with the molecules of isoamyl alcohol, make our assumption of the silver – sulfur bond even more probable.

The order of magnitude of our values for the instability constant of silver dithizonate approaches that of the instability constant for the coordination compound of silver and hydrogen sulfide recently obtained by Treadwell and Hepenstrick [4].

SUMMARY

1. The λ_{max} of the absorption spectra of the inner complex salts: silver, mercury, lead, copper, zinc, cadmium, and bismuth dithizonates, dissolved in isoamyl alcohol, have been measured and compared.

2. The Babko and Pilipenko method has been used to determine the instability constants of silver, mercury, copper, zinc, lead, and bismuth dithizonates, and these constants have been compared.

3. The relationship between the λ_{max} of dithizonates dissolved in isoamyl alcohol and their instability constants has been established.

4. The method of photographic spectrophotometry has been employed to determine the composition of AgD, and a suggestion is put forward concerning the possible structure of this inner complex salt.

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Received May 8, 1950

All Union Chemical Reagent Research Institute

RESEARCH ON ACID CATALYSTS

I. THE KINETICS AND REACTION MECHANISM OF FORMALDEHYDE IN AQUEOUS ACID SOLUTIONS

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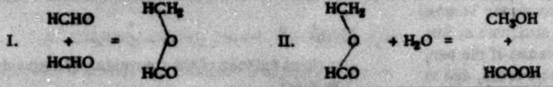
The conversion of aqueous solutions of formaldehyde to methanol and formic acid, which is frequently considered to be an oxidative-reduction reaction, may be effected in the presence of an alkali (as Cannizzaro [1], Meyer [2], Raikov and Reshtanov [3], and other research workers have observed in the case of other aldehydes) as well as in acid media.

As far back as 1883 Tishchenko [4] heated formaldehyde for a long time in sealed tubes together with strong hydrohalic acids and obtained formic acid and methyl halides. He later found that a reaction with 10% hydrochloric acid yielded formic acid and methanol itself, the reaction not proceeding to completion, part of the formaldehyde being recovered untreated even after heating to 100° for several weeks [5]. V.E. Tishchenko is also the author of the most reasonable hypothesis to explain this reaction. In 1906, in his classical paper " On the action of aluminum alcoholates upon aldehydes" [6], Tishchenko cites the following equations, after a critical review of the numerous hypotheses put forward by various authors:



in which the initial conversion product is an ester, methyl formate. But up to the present time no data have been cited in the literature to confirm this hypothesis. Nor have any papers been published on the kinetics of this reaction in acid media. The present paper fills this gap to a certain extent.

Chemistry of the Reaction

To check the composition of the formaldehyde conversion products, a special experiment was run in a stainless steel reactor, consisting of a steel tube fitted with a jacket in which a xylene fraction was boiled, thus ensuring a temperature of 140° within the reactor.

Into the reactor we charged 458 g of an aqueous solution containing 29.0% formaldehyde (introduced as paraform) and 12% chemically pure sulfuric acid. The mixture was heated for 4 hours and then poured out and analyzed, the formaldehyde being determined iodometrically [7]. The total acidity was determined by rapid titration with 0.1 N alkali, the amount of formic acid produced being found from the difference between the titrations of the initial and final solutions. The presence of formic acid was also confirmed qualitatively by the formation of calomel when the respective fractions were treated with mercuric chloride. Then the liquid was neutralized with an excess of ammonia, which also bound a substantial proportion of the formaldehyde as hexamethylenetetramine, and then fractionated into a laboratory rectifying column with an efficiency of 60 theoretical trays under operating conditions.

The characteristics of the principal fractions are given in Table 1, which shows that they are fairly pure methyl formate, methylal, and methanol.

The composition of the small intermediate fractions, which were binary mixtures, was determined by chemical analysis and by their refractive indexes. These findings are given in Table 2 as a material balance. The balance indicates that methylal is produced as follows:

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[1]) S.P. Rabinovich assisted in the experimental work.

TABLE 1

Characteristics of the Principal Fractions Collected During the Fractionation of the Reaction Products Into a Rectifying Column

		Fractions		
		Methyl formate	Methylal (azeotropic)	Methanol
Boiling point	present research	31.5-32.0°	40.7-41.5°	63.5-64.0°
	data in the literature	31.8°[8]	42.05° [20]	64.5° [8]
Specific gravity d_4^{20}	present research	0.9677	0.8651	0.7907
	data in the literature	0.975	0.862 [1]	0.792
Refractive index n_D^{20}	present research	1.3435	1.3519	1.3292
	data in the literature	1.344	1.3534 [1]	1.329
Wt. % of the principal component by chemical analysis	present research	98.0 [9]	not measured	99.5 [7]

$$CH_2O + 2CH_3OH \longrightarrow CH_2(OCH_3)_2 + H_2O.$$

in addition to the major reactions given above.

Furthermore, comparison of the quantities of free formic acid and methanol (both free and combined as methylal) indicates that they are equivalent within the limits of experimental error. Thus, 0.66 mole of HCOOH was found in the reaction product, while the amount of methanol totaled: $0.492 + 2 \cdot 0.054 = 0.60$ mole.

The slight discrepancy between these two figures is attributable, first to a certain exaggeration of the percentage of formic acid found, due to partial saponification of the methyl formate when titrated with alkali, and second to losses of the highly volatile methylal.

Even higher losses are to be counted on in the case of methyl formate, the boiling point of which (32°) is close to room temperature. Hence, much of the loss of formaldehyde in the material balance may be due to the $HCOOCH_3$, the quantity of which is correspondingly low in Table 1. Moreover, some of the formaldehyde may be converted into paraformaldehyde, which is not determined in the usual iodometric analysis for formaldehyde.

TABLE 2

Chemical Balance of the Conversion of Formaldehyde at 140° with 12% H_2SO_4

Fed in	Quantity		Produced	Quantity		CH_2O consumed (moles)
	Grams	Moles		Grams	Moles	
CH_2O	133	4.43	$HCOOCH_3$	10.90	0.182	0.364
Including			HCOOH	30.35	0.660	0.660
converted			CH_3OH	15.70	0.492	0.492
CH_2O	60.3	2.01	$CH_2(OCH_3)_2$	4.13	0.054	0.162
Water	294.0	16.35	Water	283.0	15.70	–
			CH_2O losses ...	–	–	0.332
					Total....	2.01

Nevertheless, the relationship between the quantities of methyl formate, methanol and formic acid we have found enables us to reach certain conclusions when these figures are contrasted with the equilibrium concentrations of the conversion products.

Unfortunately, we have no data on the equilibrium constant of the hydrolysis of methyl formate at the temperature specified for our experiment. Euler [10] states, however, that the equilibrium concentrations of the constituents remain practically unchanged from 0 to 60° in the hydrolysis of esters. Moreover, Schultz [11] checked Euler's data for ethyl formate and got practically the same value for the equilibrium constant at 100° that Euler had found for 50° (0.385 as against Euler's value of 0.36).

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[1] The literature data are for pure (anhydrous) methylal.

We were thus able to employ Schultz's experimental findings [11] directly to calculate the equilibrium concentration of methyl formate under our experimental conditions, i.e., at 140°; Schultz measured the equilibrium constant of the system:

$$CH_3OOCH + H_2O \rightleftharpoons CH_3OH + HCOOH$$

fairly accurately at 100 ±2° throughout a wide range of water concentrations. In our high dilution, the value of $\underline{K} = 0.24$, so that the equilibrium molar quantity of methyl formate ought to be, according to Table 2:

$$[CH_3OOCH] = \frac{[CH_3OH]\,[HCOOH]}{K[H_2O]} = \frac{0.492 \cdot 0.660}{0.24 \cdot 15.7} = 0.086 \text{ g.}$$

The experimental figure of 0.182 mole is more than twice as high as the equilibrium molar concentration of methyl formate, which far exceeds any possible experimental error. And when we remember that the CH_3OOCH concentration determined analytically was evidently too low, the excess over the equilibrium concentration of methyl formate is no longer subject to any doubt.

Hence, the conversion of formaldehyde into methanol and formic acid must involve the intermediate formation of methyl formate, which is then hydrolyzed. If this were not so, the concentration of methyl formate in the reaction products could not be higher than the equilibrium concentration.

Thus, the hypothesis advanced by V.E.Tishchenko nearly half a century ago has been directly corroborated by experiment. This cuts the ground out from the formal concept referred to above that the Cannizzaro–Tishchenko reaction is an "oxidative-reduction" reaction.

Preliminary Kinetic Analysis

Two two-stage sets of reactions may be adduced as the most likely one for a Cannizzaro – Tishchenko reaction in an acid medium.

The first stage, which is common to both sets, must be the formation of a reaction coordination compound as follows:

$$\text{A.}\quad CH_2(OH)_2 + H_2SO_4 \rightleftharpoons HOCH_2OH \cdot H_2SO_4$$

which can then react with a similar coordination compound as follows:

$$\text{B}_1.\quad 2HOCH_2OH \cdot H_2SO_4 \longrightarrow CH_3OOCH + 2H_2O + 2H_2SO_4,$$

or with a free molecule of methylene glycol:

$$\text{B}_2.\quad HOCH_2OH \cdot H_2SO_4 + CH_2(OH)_2 \longrightarrow CH_3OOCH + 2H_2O + H_2SO_4.$$

In both cases we have employed the methylene glycol form rather than the aldehydic form for the formaldehyde dissolved in water. Several papers have demonstrated by cryoscopic determinations of molecular weights, and especially, spectroscopically, that the aldehyde form is practically absent in aqueous solutions [12]. For example, Schou [13] has found that the spectra of formaldehyde dissolved in hexane exhibit the characteristic frequencies of the carbonyl group $H_2C = 0$, whereas such unhydrated molecules constitute less than 0.09% of the total of formaldehyde molecules in aqueous solutions.

However, even the fully hydrated form is actually methylene glycol only in weak formaldehyde solutions (2% and less), since an equilibrium reaction involving the polymerization of the methylene glycol monomer into its polymers is set up in the solution According to Auerbach and Barzchal [14], the principal polymerization is the formation of the trimer as follows:

$$3CH_2(OH)_2 \rightleftharpoons HOCH_2OCH_2OCH_2OH + 2H_2O.$$

The equilibrium of this reaction at formaldehyde concentrations up to 30% is satisfactorily described by the equation:

$$K = \frac{[CH_2(OH)_2]^3}{[HO(CH_2O)_3H]\,[H_2O]^2} = 0.026,$$

where $\underline{K} = 0.026$ is the equilibrium constant at 20°.

The equilibrium concentrations of the monomer – methylene glycol – calculated for aqueous solutions at 20° are given in Table 3.

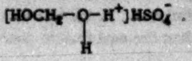
TABLE 3

Concentrations of Methylene Glycol in Mixtures with Trioxymethylene Glycol in Aqueous Solutions at 20°

Per cent concentration of formaldehyde in water	2.4	5.9	11.2	21.1	28.2	33.8
Per cent of formaldehyde as methylene glycol.........	98	87	72	53	41	33

The figures in Table 3 indicate that the concentration of the monomer is fairly high at 20° for all the concentrations of formaldehyde solutions that are attainable in practice. At higher temperatures the state of equilibrium must be shifted toward dissociation, as is the case in other polymerization reactions. We may therefore assume, as a first approximation, that at the temperatures employed in the present research most of the formaldehyde occurs in the reaction liquid as methylene glycol, as indicated in the reactions set forth above.

As for the structure of the reaction coordination compound referred to above, this problem is of no account for our further discussion. What is most likely, however, is the formation of an oxonium compound, as follows:



$$[HOCH_2-\underset{H}{O}-H^+]HSO_4^- .$$

The possibility that such compounds may be formed when sulfuric acid reacts with diethyl ether has been demonstrated by the researches of V.V.Chelintsev, who secured the following coordination compounds:

$$(C_2H_5)_2O \cdot H_2SO_4 \quad \text{and} \quad 2(C_2H_5)_2O \cdot H_2SO_4$$

as far back as 1914 and determined their heats of formation [15]. Subsequently, the actual existence of these coordination compounds was convincingly proved by Usanovich, Sabinina, and Zavarikhina [16], who made a comprehensive study of the physicochemical properties of the ether + sulfuric acid and water + sulfuric acid systems.

Kendall and his co-workers established that oxonium coordination compounds are formed by sulfuric acid with alcohols, using as their examples the higher phenols: o-$(CH_3)_2C_6H_3OH \cdot H_2SO_4$ and p-$(CH_3)_2C_6H_3OH \cdot H_2SO_4$ [17].

We still have no corresponding data in the literature for the aliphatic alcohols, though the systematic researches of V.V.Chelintsev on the heat involved in the formation of coordination compounds of various oxygen-containing compounds with organo-magnesium alcoholates enable us to reach certain conclusions in this respect as well.

V. V. Chelintsev's findings [18] on the heats of formation of coordination compounds of the initial molecules of some alcohols and diethyl ether with C_2H_5OMgI and sulfuric acid are given in Table 4.

TABLE 4

Heats of Formation of Some Oxonium Compounds According to V. V. Chelintsev [18]

Compound	Central group in the coordination compound	Heat evolved by the addition of the initial molecule, cal·mole
Methanol.............	C_2H_5OMgI	11.60
Ethyl alcohol........		12.78
Isopropyl alcohol...		8.88
Phenol................		5.06
Diethyl ether........	C_2H_5OMgI	5.05
Diethyl ether........	H_2SO_4	6.87

Inspection of Table 4 indicates that the heat evolved by addition of C_2H_5OMgI to diethyl ether is close to that involved in the addition of sulfuric acid. By analogy it may be assumed that the heat of formation of an oxonium coordination compound of primary alcohols and sulfuric acid will likewise approach the heat of formation of a coordination compound containing C_2H_5OMgI. This thermal effect for the primary alcohols is more than twice that for a coordination compound with the ether.

Hence, strong bonds may be established by the higher valencies of the oxygen in the hydroxyl group in the alcohols, these bonds producing a fundamental change in the electronic structure of the $CH_2(OH)_2$ molecule in an oxonium coordination compound, and this is responsible for the substantial activation of the methylene group. This makes the latter able to enter into a reaction either with another similarly activated molecule of the oxonium coordination compound or with an ordinary methylene glycol molecule, these two alternatives constituting the two reaction mechanisms set forth above.

The ionic nature of the reaction involved in the formation of the oxonium coordination compound in an aqueous solution leads us to conclude that methylene glycol reacts extremely rapidly with sulfuric acid. We therefore assume that the first stage common to both sets of reactions proceeds until equilibrium is practically achieved, as defined by the equation:

$$K_C = \frac{[CH_2(OH)_2 \cdot H_2SO_4]}{[CH_2(OH)_2][H_2SO_4]} = \frac{z}{(a - z)(b - z)} \quad . \tag{1}$$

where K_C is the equilibrium constant; $\underline{z}$ is the concentration of the coordination compound; and $\underline{a}$ and $\underline{b}$ are the total concentrations of methylene glycol and sulfuric acid, respectively. The symbols in brackets are the respective equilibrium concentrations of the reaction components.

But when the concentration of the oxonium coordination compound is not very high, compared to the total amount of methylene glycol present (which actually is the case, as will be shown later), Equation (1) may be simplified as follows:

$$K_C = \frac{z}{a(b - z)} \quad , \tag{2}$$

whence the concentration of the reaction coordination compound is:

$$z = \frac{ab}{a + \frac{1}{K_C}} \quad , \tag{3}$$

Equation (3) may be used to set up the kinetic equation for both of the postulated sets of reactions. Starting with the stiputlated assumption that the controlling reaction rates will be those of the second process stages, we get the corresponding equations.

Mechanism I yields the equation:

$$\frac{dx}{d\tau} = k'' \,[CH_2(OH)_2 \cdot H_2SO_4]^2 = k'' \frac{a^2 b^2}{\left(a + \frac{1}{K_C}\right)^2} \quad , \tag{4}$$

where $\underline{k}''$ is the constant of action of B_1.

Introducing the following notation: a_0 for the initial amount of methylene glycol per unit of solution, $C_{H_2SO_4}$ for the concentration of sulfuric acid, $\underline{x}$ for the amount of methylene glycol converted in time τ, and $y = x/a_0$ for the proportion of the methylene glycol converted in time τ, we obtain the following differential equation:

$$a_0 \frac{dy}{d\tau} = k'' \, C^2_{H_2SO_4} \frac{(1 - y)^2}{\left(1 - y + \frac{1}{a_0 K_C}\right)^2} \quad , \tag{4a}$$

integration of which yields the general form of equation for the constant of action $\underline{k}''$:

$$k'' = \frac{1}{C^2_{H_2SO_4}\tau} \left[a_0 y + \frac{4.6}{K_C} \log \frac{1}{1 - y} + \frac{y}{a_0 K_C^2 (1 - y)}\right] . \tag{5}$$

Mechanism II yields the initial equation:

$$\frac{dx}{d\tau} = k' \,[CH_2(OH)_2 \cdot H_2SO_4]\,[CH_2(OH)_2] = k' \frac{a^2 b}{a + \frac{1}{K_C}} \tag{6}$$

whence, by analogy with the preceding derivation, we secure

$$\frac{dy}{d\tau} = k' \, C_{H_2SO_4} \frac{(1 - y)^2}{1 - y + \frac{1}{a_0 K_C}} \tag{6a}$$

integration of which yields the general equation

$$k' = \frac{1}{C_{H_2SO_4}\tau}\left[2.3\log\frac{1}{1-y} + \frac{y}{a_0K_C(1-y)}\right]. \qquad (7)$$

Inspection of Equations (5) and (7) yields the following conclusions.

1. In both cases the reaction rate may be monomolecular at high values of the equilibrium constant K_C and bimolecular at extremely low values of K_C. This conclusion follows from the presence in Equations (5) and (7) of terms, the last of which correspond to an expression for a second-order reaction, while the preceding ones correspond to that for a first-order reaction. The ratio between these two terms will vary widely with the value of K_C, and in the extreme cases the terms that become extremely small may be neglected.

2. When the reaction follows the patern of Mechanism I, as specified by Equation (5), the rate at which the formaldehyde is converted must be proportional to the square of the sulfuric acid concentration, whereas when the reaction is of the Mechanism II type, as specified by Equation (7), the rate must be proportional to the first power of the sulfuric acid concentration. In the intermediate case, i.e., when the reaction is mixed, with both types present at the same time, we must have, formally speaking, a fractional order of reaction with respect to acid.

Procedure Used for Kinetic Measurements

The tests were run in sealed glass ampoules, with a capacity of approximately 10 ml, into which a solution of pure paraform in distilled water was introduced together with a measured quantity of chemically pure sulfuric acid.

In preliminary tests, the ampoules were heated on water or glycerol baths, the temperature of which differed from the given temperature by 3 to 5° in individual instances In the precise kinetic experiments we employed an ultrathermostat in which the temperature fluctuations did not exceed 0.2°C.

The ampoules were taken out of the thermostat at given intervals of time, quickly cooled, and their contents analyzed.

The formaldehyde was determined iodometrically [7], the formic acid being determined by the difference between the titrations of the reacted and initial solutions.

Kinetic Data and Their Evaluation

The results of our preliminary tests, made with less precise temperature control, are given in Table 5.

All the converted formaldehyde is listed in Column 5, Column 6 gives the amount of formaldehyde converted into formic acid. Comparison of these figures indicates that much of the methyl formate formed initially is subjected to very deep hydrolysis in all cases, as was observed in the balance test described by us.

Since it is difficult to use the derived general Equations (5) and (7) directly because of the absence of the values of the constant K_C, we employed simpler expressions in working up the experimental data of Table 5, which describe the special cases referred to in the preliminary kinetic analysis of the greatest and smallest values of the equilibrium constant, i.e., for $K_C \gg 1$.

Mechanism I: $$k_1^{I'} = \frac{a_0 y}{C^2_{H_2SO_4}\tau}; \qquad (8)$$

Mechanism II: $$k_1^{II} = \frac{2.3}{C_{H_2SO_4}\tau}\log\frac{1}{1-y} \qquad (9)$$

for $K_C \ll 1$.

Mechanism I: $$k_2^{I'} = \frac{y}{C^2_{H_2SO_4}a_0\tau(1-y)} \qquad (10)$$

Mechanism II: $$k_2^{II} = \frac{y}{C_{H_2SO_4}a_0\tau(1-y)} \qquad (11)$$

where $C_{H_2SO_4}$ is the concentration of sulfuric acid in moles per 100 grams; a_0 is the initial concentration of formaldehyde in moles per 100 grams; τ is the time in hours. The values of the velocity constants computed from these equations (cf. Table 5) indicate that Equations (8) and (9), dealing with $K_C \gg 1$, are entirely unsuitable to describe the reaction kinetics, inasmuch as the values of the constant rise sharply with increasing initial

TABLE 5

Kinetics of the Conversion of Formaldehyde in Aqueous Acid Solutions (Preliminary Tests)

No. of determination	Temperature	Time, hours (τ)	Concentration, wt. %: Acid in terms of H_2SO_4	Concentration, wt. %: CH_2O	Formaldehyde consumed, moles/100 g: Total $CH_2(OH)_2$	Formaldehyde consumed, moles/100 g: In terms of HCOOH	Converted proportion of $CH_2(OH)_2$, y	Constants of action: Monomolecular: $k_1''\cdot10$, Equation (8)	Constants of action: Monomolecular: $k_1'\cdot10$, Equation (9)	Constants of action: Bimolecular: $k_2''\cdot10$, Equation (10)	Constants of action: Bimolecular: $k_2'\cdot10$, Equation (11)	Constants of action: Mixed: $k_2'''\cdot10$, Equation (14)
1		2	3	4	5	6	7	8	9	10	11	12
1	100°	0	6.35	14.1	–	–	–	–	–	–	–	–
		20	6.70	13.9	0.006	0.014	0.013	0.7	1.1	3.3	2.2	0.6
		40	6.95	13.3	0.026	0.024	0.055	1.5	2.1	7.3	4.7	1.4
		80	7.25	12.9	0.040	0.036	0.085	1.2	1.8	5.8	3.8	1.1
							Average	1.0	1.7	5.5	3.6	1.0
2	100°	0	6.25	28.5	–	–	–	–	–	–	–	–
		20	6.50	27.5	0.032	0.010	0.034	3.9	2.7	4.5	2.9	0.9
		40	7.75	26.1	0.080	0.080	0.084	4.9	3.4	5.9	3.7	1.2
		80	8.05	24.9	0.120	0.072	0.126	3.7	2.6	4.6	3.0	0.9
							Average	4.2	2.9	5.0	3.2	1.0
3	100°	0	13.50	12.7	–	–	–	–	–	–	–	–
		40	14.45	11.3	0.048	0.040	0.113	0.6	2.2	3.9	5.4	1.2
		80	14.85	10.4	0.078	0.056	0.184	0.5	1.8	3.5	4.9	1.1
							Average	0.6	2.0	3.7	5.2	1.1
4	100°	0	14.60	26.25	–	–	–	–	–	–	–	–
		40	17.00	19.70	0.218	0.098	0.248	2.5	4.8	4.3	6.3	1.3
		80	18.60	18.40	0.262	0.164	0.299	1.5	3.0	2.8	4.2	0.9
							Average	2.0	3.9	3.5	5.2	1.1
5	100°	0	14.35	28.05	–	–	–	–	–	–	–	–
		40	16.05	23.65	0.146	0.070	0.156	1.7	2.9	2.3	3.4	0.7
		80	18.85	17.95	0.336	0.184	0.359	1.9	3.7	3.4	5.1	1.1
							Average	–	3.3	2.9	4.3	0.9
6	120 - 130°	0	14.50	14.05	–	–	–	–	–	–	–	–
		16	17.70	7.70	0.212	0.132	0.453	–	–	50	74	16
7	135°	0	14.50	13.40	–	–	–	–	–	–	–	–
		1.25	15.80	11.40	0.066	0.052	0.148	–	–	140	210	44
		2.25	16.40	10.80	0.086	0.076	0.193	–	–	110	160	35
		3.25	16.70	9.30	0.136	0.088	0.305	–	–	140	210	44
		4.25	17.50	8.50	0.162	0.122	0.363	–	–	135	200	44
							Average	–	–	130	195	42

concentration of the formaldehyde (cf Tests 1, 2, and 3-5). The bimolecular Equations (10) and (11) yield a satisfactory constancy of the constant (cf the same tests) for the tests with similar concentration of sulfuric acid. Neither of the foregoing equations is satisfactory for describing the quantitative relationship between the reaction rate and the acid – catalyst concentration. Thus, the value of k_2'' as computed from Equation (10), dealing with a second-power variation with $C_{H_2SO_4}$, falls off with increasing acid concentration, whereas k_2', computed from Equation (11) for a linear variation with $C_{H_2SO_4}$, rises with increasing acid concentration (compare Tests 1 and 2 with 3-5).

Thus the kinetic order of reaction is fractional, formally speaking, with respect to sulfuric acid.

TABLE 6

Effect of the Concentration of Sulfuric Acid upon the Conversion of Formaldehyde in Aqueous Solution at 148.8°

Expt. No.	Time, hours (τ)	Concentration, wt. %		Formaldehyde consumed, moles/100 g		Converted proportion of $CH_2(OH)_2$, y	Constants of action		
		Acid, in terms of H_2SO_4	CH_2O	Total $CH_2(OH)_2$	In terms of HCOOH		k_2^t, Equation (11)	$k_2^{t'}$, Equation (10)	$k_2^{t''}$, Equation (14)
10	0	3.10	24.80	0	0	0	–	–	–
	9.30	12.50	10.80	0.467	0.384	0.565	5.3	168	21
	15.5	13.70	7.00	0.594	0.434	0.718	6.3	200	25
	21.3	14.65	5.80	0.634	0.472	0.767	6.0	190	24
11	0	6.25	25.00	0	0	0	–	–	–
	1.72	12.70	16.00	0.300	0.264	0.360	6.1	95	19
	3.38	15.20	11.50	0.449	0.366	0.540	6.5	102	20
	6.72	17.55	7.50	0.583	0.462	0.700	6.5	102	20
	9.30	17.85	4.50	0.683	0.476	0.820	8.2	128	25
12	0	12.50	24.50	0	0	0	–	–	–
	0.47	17.45	18.20	0.210	0.202	0.257	7.1	56	17
	0.88	19.95	13.65	0.362	0.304	0.443	8.6	67	20
	1.72	23.35	9.10	0.514	0.440	0.630	9.5	74	22
	2.80	24.30	6.50	0.601	0.482	0.736	9.6	75	22
13	0	20.50	24.50	0	0	0	–	–	–
	0.215	26.15	16.75	0.259	0.230	0.317	11	53	21
	0.385	28.40	13.15	0.379	0.324	0.464	14	67	26
	0.715	31.05	8.05	0.549	0.432	0.673	17	81	31

Special kinetic tests were run in an ultrathermostat to establish this relationship quantitatively, the results being listed in Table 6.

These findings bore out the conclusion set forth above concerning the fractional acid order of reaction, i.e., the kinetic equation ought to look like this:

$$k_2^{t''} = \frac{y}{C^{n}_{H_2SO_4} \; a_0 \tau \; (1 - y)} \,, \tag{12}$$

where n is the exponent of the kinetic order of reaction according to sulfuric acid.

Transforming (12) and taking the logarithm of both sides, we get the expression

$$n \log C_{H_2SO_4} + \log k_2^{t''} = \log \frac{y}{a_0 \tau (1 - y)} = \log A. \tag{12a}$$

Differentiation yields the equation

$$n = \frac{d \log A}{d \log C_{H_2SO_4}} \,, \tag{13}$$

where n is the slope of a straight line plotted on log A – log $C_{H_2SO_4}$ coordinates.

Graphically plotting the experimental data of Table 6 we get n = 1.4, so that Equation (12) becomes:

$$k_2^{t''} = \frac{y}{C^{1.4}_{H_2SO_4} \; a_0 \tau \; (1 - y)} \,. \tag{14}$$

We used this last equation to calculate the constants of action in the last column of Table 6.

The values of $k_2^{t''}$ thus calculated, as listed in Table 6, are satisfactorily constant for adjacent percentage conversions of formaldehyde throughout a wide range of sulfuric acid concentrations.

From these figures we may conclude that under the experimental conditions employed the process apparently follows both of the postulated sets of reactions, 40% of the reaction taking place as an interaction between two active coordination compounds.

When we consider the course of the variable k_2''' in each of the experiments, however, we note that it rises regularly as the process continues; this might be due to the error introduced by our using Equation (14) instead of general Equations (5) and (7) for the special case when the equilibrium constant K_C is extremely small.

To test this assumption we ran tests with varying initial concentrations of formaldehyde, the results of which are listed in Table 7.

TABLE 7

Effect of the Initial Concentration of Formaldehyde Upon the Conversion of the Latter in an Aqueous Solution at 148°.

Test No.	Time, hours (τ)	Concentration, wt. %		Formaldehyde consumed, moles/100 g		Converted proportion of $CH_2(OH)_2$, y	Constants of action	
		Acid, in terms of H_2SO_4	CH_2O	Total $CH_2(OH)_2$	In terms of HCOOH		k_1'', Equation (15)	k_2''', Equation (14)
14	0	12.05	10.30	0	0	0	–	–
	0.7	13.60	8.50	0,060	(0.064)	0.175	5.1	17
	1.4	14.65	7.15	0,105	(0.116)	0.306	4.9	17
	2.8	15.80	5.05	0.175	0.152	0.510	4.8	20
	5.6	16.75	3.25	0.235	0.192	0.685	3.9	21
15	0	12.25	13.45	0	0	0	–	–
	0.5	14.30	11.40	0.068	(0.084)	0.152	6.1	15
	1.0	15.55	9.50	0.131	(0.136)	0.292	6.4	17
	2.0	17.05	6.80	0.221	0.196	0.493	6.2	20
	3.8	18.50	4.60	0.295	0.256	0.658	5.1	21
16	0	12.35	27.30	0	0	0	–	–
	0.25	16.10	22.75	0.152	0.152	0.167	13.5	16
	0.5	18.85	18.60	0.290	0.266	0.318	14.0	19
	1.0	21.85	13.70	0.453	0.288	0.498	12.5	20
	2.0	24.35	8.65	0.622	0.490	0.683	10.5	22

TABLE 8

Effect of Temperature upon the Rate of Conversion of Formaldehyde in the Cannizzaro – Tishchenko Reaction in Acid Solutions

Test No.	Temperature	k_2'''	Log $k_2''' \cdot 10$		E cal/mole	Temperature coefficient in vicinity of 100°
			Found	Calculated		
1-5	100°	0.1	0.00	0.00	32900	3.3
6	120 - 130	1.6	1.20	1.20 1)		
7	135	4.2	1.62	1.65		
10-16	148.8	17	2.23	2.23		

The last column in Table 7 gives the constants k_2''', calculated from Equation (14) as before. In the next to the last column we have listed the values of the constant k_1'' as given by the equation

$$k_1'' = \frac{2.3}{\tau C_{H_2SO_4}^{1.4}} \log \frac{1}{(1-y)} \qquad (15)$$

that stems from Equation (7) for $K_C \gg 1$.

As indicated by the results of our preliminary tests, listed in Table 5, however, the monomolecular Equation (15) is refuted by the experimental data, since k_1'' falls proportionally to the decreasing initial concentration of formaldehyde.

The bimolecular constants k_2''', for the same percentage conversions of formaldehyde, remain constant, as in the preceding tests, when the initial formaldehyde concentration is varied from 0.34 to 0.91 mole per 100 grams, i.e., by a factor of 2.7.

Hence, the general Equations (5) and (7) derived theoretically may be replaced by Equation (14) with a high degree of accuracy in the given case, which excludes the likelihood that the assumption made above is correct.

---

1) Calculated for the mean temperature of 125°.

Another possible explanation of the rise of k_2''' with increasing percentage conversion of the formaldehyde was the presupposition of autocatalysis, say, as the result of the catalytic influence of the formic acid formed in the reaction, as this acid might also be able to form oxonium compounds with methylene glycol. We know of such compounds of phenol with chloroacetic acid, for example [19].

However, there is no such effect in the present case, apparently. This is borne out by the fact that the rise in the k_2''' constant with percentage conversion is no larger at low concentrations of sulfuric acid than in the tests at high concentrations of sulfuric acid (see Table 6). Hence, a pronounced increase in acidity due to the formic acid produced (by a factor of 4.7 in Test 10) has very little effect upon the overall reaction rate.

Therefore, the most likely reason for the rise in the value of the constant with increasing percentage conversion is the occurrence of secondary conversions of the formaldehyde, the most important being the formation of methylal.

As we have said, this conclusion agrees with the analytical data on the composition of the reaction products in the balance test run at a high percentage of conversion (Table 2).

It follows that the true constants of action are the lower values calculated from Equation (14), corresponding to low percentages of conversion of formaldehyde, when the methanol concentrations are still low and only very little methylal has been formed.

We used Equation (14) to calculate the constants for the experiments described in Table 5; they also remain satisfactorily constant within the limits of accuracy of the preliminary measurements throughout all the tests made at 100°.

This made it possible to use all the tests run in the present research to derive an approximate temperature coefficient of the reaction rate in the given range of experimental conditions.

To do this, we used (of the data in Table 5) the arithmetical mean of the experimental values of the constant k_2''', which rose less with time in this case, since most of the tests listed in Table 5 were run at a comparatively low percentage conversion, while for the temperature of 148.8° we took the minimum mean values of k_2''', in accordance with the argumentation set forth above.

These mean values are listed in Table 8, together with the results obtained by working them up.

The values of the velocity constant tabulated in Table 8 lie on a straight line when plotted on $\log k_2''' - \frac{1}{T}$ coordinates (see Figure), so that we get the equation

$$\log k_2''' = 18.30 - \frac{7200}{T}, \qquad (16)$$

where T is the absolute temperature.

The high value of the activation energy – 33 kcal/mole – and the correspondingly high temperature coefficient of the reaction rate – 3.3 – indicate the existence of a substantial energy barrier that the reacting molecules have to overcome even when only active coordination compounds interact. Unfortunately, the figures in Table 5 do not enable us to determine the value of n with sufficient accuracy for the order of the reaction in terms of acid at 100°. This makes it impossible as yet to evaluate quantitatively the difference between the activation energy of the reaction of the oxonium coordination compounds with the free methylene glycol molecule and that of the reaction between the oxonium compounds themselves. The satisfactory way in which Tests 1-2 and 3-5 follow Equation (14) indicates, however, that at 100° the value of n_{100} can hardly be much greater than $n_{149} = 1.4$ for 149°. Hence, it is hard to expect any appreciable difference in the values of E for the two reactions.

As for the comparative reaction rates of the active coordination compounds with the methylene glycol in the free and combined state, we can make an approximate calculation therefor.

In view of the proof that we can shift from the general equations (5) and (7) to the bimolecular Equation (14) without introducing any perceptible error, we may conclude that the magnitude of the equilibrium constant of the formation of a coordination compound must be extremely small. Thus, if we use Equation (7), for example, its first term may be ignored only at $K_C < 0.1$ according to the order of experimental error involved.

If we adopt this last value, we get from Equation(1)

$$[CH_2(OH)_2 \cdot H_2SO_4] = 0.1[CH_2(OH)_2][H_2SO_4], \qquad (17)$$

whence, substituting the mean values of the concentrations of methylene glycol and sulfuric acid used in the present research (in moles per 100 grams), we get the concentration of the active coordination compound as

$$[CH_2(OH)_2 \cdot H_2SO_4] = 0.1 \cdot 0.5 \cdot 0.15 = 0.0075 \text{ mole/100 grams.}$$

No more than 5% of the total acid or 1.5% of the formaldehyde is combined in the active coordination compound. The latter figure bears out the correctness of the simplification effected above in shifting from Equation (1) to Equation (2). Using these concentrations of the constituents of the reaction mixture, we can make an approximate calculation of the constants: k_1 for the B_1 reaction and k_2 for the B_2 reaction. Inserting the values derived above: $C_\Phi = 0.5$ mole/100 g, $C_{H_2SO_4} = 0.15$ mole/100 g and $C_K = 0.0075$ mole /100 g, in the equation

$$k_2''' \, C^{1.4}_{H_2SO_4} \, C^2_\Phi = k_1 C^2_K + k_2 C_K C_\Phi \qquad (18)$$

$$\frac{k_1 C^2_K}{k_2 C_K C_\Phi} = \frac{40}{60}\,, \qquad (19)$$

we get the following values for the constants of action in the respective reactions at 148.8°, corresponding to $k_2''' = 17$:

$$k_1 = 2000,\ k_2 = 50 \text{ and } \frac{k_1}{k_2} = 40.$$

Thus, as might have been expected, the velocity of interaction between the molecules of the active coordination compound is many times greater than the velocity of the reaction of the coordination compound with the free molecule of methylene glycol.

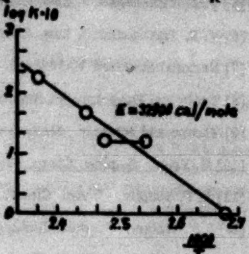


Figure. Variation of k_2''' with temperature.

SUMMARY

1. It has been shown experimentally that the actual concentration of methyl formate in the reaction products substantially exceeds its equilibrium percentage, which confirms V.E.Tishchenko's assumption that the reaction involves the intermediate formation of an ester.

2. A two-stage mechanism is put forward for the Cannizzaro-Tishchenko reaction, the velocity of which is governed by the following parallel reactions:

$$2CH_2(OH)_2 \cdot H_2SO_4 \rightarrow HCOOCH_3 + 2H_2O + 2H_2SO_4;$$

$$CH_2(OH)_2 \cdot H_2SO_4 + CH_2(OH)_2 \rightarrow HCOOCH_3 + 2H_2O + H_2SO_4.$$

3. Kinetic equations are derived to describe the velocity of the principal reaction over a wide range of experimental conditions.

4. The activation energy of the reaction $E = 32{,}900$ cal/mole, corresponds to a temperature coefficient of the reaction rate of 3.3 in the proximity of 100°.

5. The order of magnitude of the equilibrium constant for the formation of the active coordination compound has been determined to be

$$K_c < 0.1,$$

from which it follows that only little of the acid or the formaldehyde is combined in the coordination compound in the reaction mixture.

6. The approximate ratio of the velocity constant of the interaction between the active coordination compounds themselves (k_1) to that of the coordination compound with a free molecule of methylene glycol has been calculated as (k_2): $k_1/k_2 = 40$.

7. It has been shown that the principal reaction is paralleled by the formation of methylal as a result of the interaction of the formaldehyde with the methanol produced.

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Received May 30, 1950

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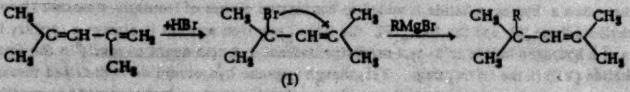
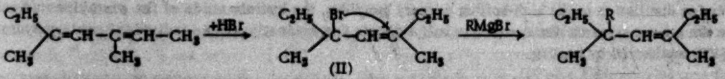
SYNTHESIS OF HYDROCARBONS

XVIII. THE HYDROBROMIDE AND HYDROCHLORIDE OF 2-METHYLPENTADIENE-1,3 AND 4-METHYLPENTADIENE-1,3 IN THE SYNTHESIS OF HYDROCARBONS OF ISOMERIC STRUCTURE

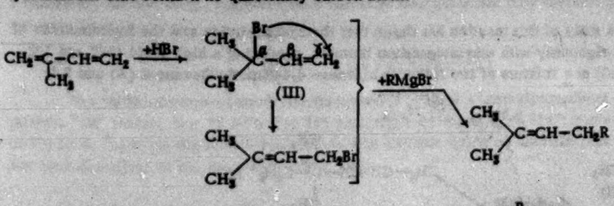
R. Ya. Levina, A. A. Fainzilberg, and E. G. Treshchova

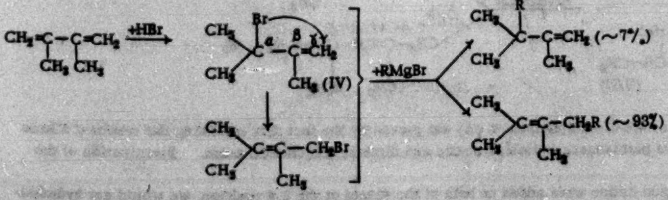
In previous papers one of the present authors has described a method of synthesizing hydrocarbons with a quaternary carbon atom, based upon the reactions of organomagnesium compounds with hydrobromides of diene hydrocarbons — 2,4-dimethylpentadiene-1,3 [1] and 3,5-dimethylpentadiene-2,4 [2]. The hydrobromides of these dienes are alike in these respects: they are unsaturated tertiary bromides (I and II) and homologs of allyl bromide, while their structure renders an allyl rearrangement impossible:



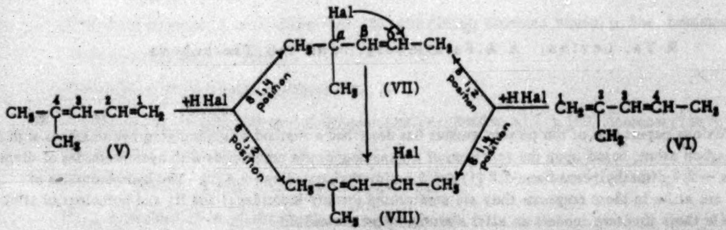


Tertiary hydrobromides (or hydrochlorides) can also be prepared from other dienes of isomeric structure: isoprene [3-6], 2,3-dimethylbutadiene-1,3 [5-7 and others]. In contrast to the tertiary unsaturated bromides cited above, however, these tertiary unsaturated bromides (III and IV), undergo allyl rearrangement into isomeric primary bromides readily when heated or when subjected to any chemical transformation. Isoprene hydrobromide, for example, reacts with organo-magnesium compounds only in its primary form, and not in its tertiary form [5,8]; 90 % of 2,3-dimethylbutadiene-1,3 hydrochloride (or hydrobromide) likewise enters into a reaction of this sort in its primary form [5,9]. Hence, the principal products of these reactions are hydrocarbons that contain no quaternary carbon atom:





The present paper is a report of an investigation of the reaction of an organo-magnesium compound with the hydrobromide (and the hydrochloride) of 4-methylpentadiene-1,3 and 2-methylpentadiene-1,3. The addition of hydrogen bromide or chloride to these dienes (V and VI) at the 1,2 or 1,4[1] position ought to result in the formation of hydrohalides that can exist, (like the hydrobromides of isoprene and of 2,3-dimethylbutadiene) in two isomeric forms related to an allyl rearrangement: as an unsaturated tertiary halide (VII) and as an isomeric secondary one (VIII):



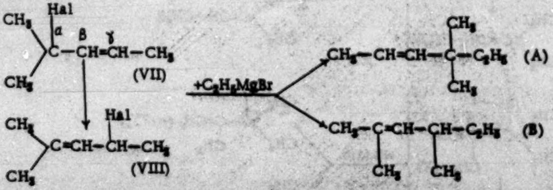
$CH_3-\overset{4}{C}=\overset{3}{C}H-\overset{2}{C}H=\overset{1}{C}H_2$
CH_3
(V)
+H Hal
at 1,4 position
at 1,2 position
Hal
α β γ
$CH_3-C-CH=CH-CH_3$
CH_3
(VII)
Hal
$CH_3-C=CH-CH-CH_3$
CH_3
(VIII)
at 1,4 position
at 1,2 position
+H Hal
$\overset{1}{C}H_2=\overset{2}{C}-\overset{3}{C}H=\overset{4}{C}H-CH_3$
CH_3
(VI)

We know that when a hydrogen halide is added to conjugated dienes of isomeric structure (isoprene [3,5,6], 2,3-dimethylbutadiene [6], and the like [10], the initial reaction product is always a tertiary halide, hence, the addition of a hydrogen halide to 2- or 4-methylpentadiene-1,3 also ought to result in the formation of a tertiary hydrohalide (VII) in the initial stage. Yet, though isoprene hydrobromide is distilled through a wide temperature range (twenty degrees) [5,8,11] (since the low-boiling tertiary hydrobromide is readily isomerized during distillation to the high-boiling primary bromide), the hydrobromide of the methylpentadienes secured in the present research distilled within half a degree and evidently was an individual tertiary hydrobromide (VII) unaffected by heating.

Nor was the hydrochloride of the methylpentadienes affected by repeated distillation, or by the action of an excess of hydrogen chloride, i.e., by the conditions in which the tertiary isoprene hydrochloride is rearranged into the isomeric primary compound [3].

The location of the methyl radical at the γ -position to the active halogen atom is a characteristic feature of the structure of the tertiary methylpentadiene hydrobromide and hydrochlorides (VII); this should explain their high stability and reactivity, compared to the tertiary hydrobromides of isoprene and 2,3-dimethylbutadiene (III, IV). We might, therefore, expect the products of the reaction of the hydrohalides of 2- or 4-dimethylpentadiene-1,3 with an organomagnesium compound to contain a high percentage of an alkene with a quaternary carbon atom.

As a matter of fact, a study of this reaction has shown that the hydrochloride and the hydrobromide of the methylpentadienes react vigorously with ethylmagnesium bromide, producing a high yield (50% and 70%, respectively of the theoretical) of a mixture of two isomeric alkenes—4,4-dimethylhexene-2 (A) and 2,4-dimethylhexene-2 (B):



Hal
α β γ
$(CH_3)_2C-CH=CH-CH_3$
(VII)
Hal
$(CH_3)_2C=CH-CH-CH_3$
(VIII)
$+C_2H_5MgBr$
$CH_3-CH=CH-C(CH_3)_2-C_2H_5$ (A)
$CH_3-C(CH_3)=CH-CH(CH_3)-C_2H_5$ (B)

The presence of 4,4-dimethylhexene-2 (A) was proved by the fact that oxidizing the resultant alkene mixture with potassium permanganate yielded acetic and dimethylethylacetic acids. Bromination of the mixture gave us a 50% yield of a stable dibromide, as is typical for a symmetrical disubstituted homolog of ethylene, which is what 4,4-dimethylhexene-2 (A) is; this was further confirmation of its presence in the alkene mixture we had produced. The presence of 2,4-dimethylhexene-2 (B) in this mixture was proved by our securing acetone peroxide—the most characteristic product of the ozonidation of 2,4-dimethylhexene-2—when we ozonized the mixture. Investigation of the Raman spectrum of the alkene mixture yielded an interesting conclusion regarding the geometrical configuration of 4,4-dimethylhexene-2 (A), namely: this hydrocarbon had a *trans* configuration, so that the initial tertiary hydrohalide (VII) was a pure *trans* form:

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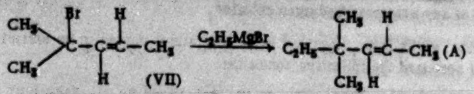
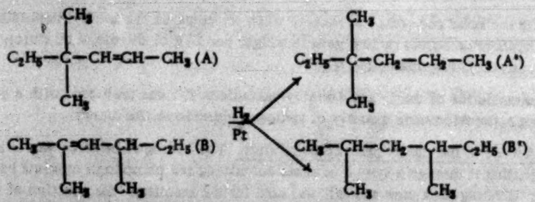
[1] If the hydrogen halide were added to both of the dienes at the 3,4 position, we would get hydrohalides that did not belong to the allyl halide series and would not react with organomagnesium compounds under ordinary conditions.



The quantitative composition of the alkene mixture we were investigating was established by hydrogenating them and comparing the Raman spectrum of the resultant mixture of alkanes with the spectra of the two components of that mixture: 3,3-dimethylhexane (A') and 2,4-dimethylhexane (B'):



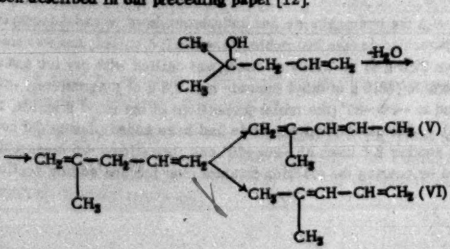
This spectroscopic examination indicated that the resultant alkane mixture contained some 40% of 3,3-dimethylhexane (A') and some 60% of 2,4-dimethylhexane (B'); hence, the original mixture of alkenes contained the same proportion of the respective alkenes, namely: some 40% of 4,4-dimethylhexene-2 (A) and some 60% of 2,4-dimethylhexene-2 (B).

Therefore, the tertiary allyl halides (the hydrobromide and the hydrochloride of 2- or 4-methylpentadiene-1,3), which possess a methyl group in the δ-position to the active halogen atom (VII), are much more stable than other tertiary allyl halides (the hydrobromides or hydrochlorides of isoprene and of 2,3-dimethylbutadiene), which do not possess this sort of structure (III and IV).

The stability of the tertiary hydrohalides (VII) of 2- or 4-methylpentadiene-1,3 in reactions with organomagnesium compounds makes it possible to use these halides for synthesizing hydrocarbons containing a quaternary carbon atom, irrespective of the allyl rearrangement they frequently experience in the course of the reaction.

EXPERIMENTAL

The initial dienes—2-methylpentadiene-1,3 (V) and 4-methylpentadiene-1,3 (VI)—were prepared as a mixture (59% yield); b.p. 72.5-75.5° at 761 mm, n_D^{20} 1.4474 and d_4^{20} 0.7147; containing 30-35% of V and 65-70% of VI by dehydrating dimethylallylcarbinol with chromic oxide on alumina (the preparation of these dienes has been described in our preceding paper [12].



Addition of hydrogen chloride to the mixture of methylpentadienes. This reaction was carried out under conditions that excluded the possibility of an allyl rearrangement of the resultant tertiary allylic chloride (VII) (4-chloro-4-methylpentene-2), i.e., with deep chilling and the introduction of less hydrogen chloride than called for by the equation [3]. The reaction vessel was chilled to −20-−25°, and 17 g (about 0.2 mole) of the methylpentadiene mixture was placed in it together with 2-3 g of absolute ether (to insure better dissolution of the hydrogen chloride); hydrogen chloride was added until the gain in weight totaled 5 g (0.14 mole). Then a current of anhydrous nitrogen was passed through the reaction mixture, deeply chilled (to −70 or −80°), to remove all traces of any unreacted hydrogen chloride.

The synthesized hydrochloride (which is not described in the literature) proved to be entirely stable—it distilled within half a degree and possessed the following constants:

B.p.46.5-47° (83 mm); n_D^{20} 1.4438; d_4^{20} 0.8969 MR_D 35.12; calculated 34.31; EM_D 0.81 (the presence of exaltation of the molecular refraction is a characteristic of allylic halides). The percentage of chlorine in the hydrochloride was determined by the M.O.Korshun and M.N.Chumchenko method [13]: 2.5600 mg substance: 1.077 ml 0.02 N $AgNO_3$; 1.4589 mg substance: 0.6106 ml 0.02 N $AgNO_3$. Found %: Cl 29.82, 29.66. $C_6H_{11}Cl$; Calculated %: Cl 29.90.

A hydrochloride with the same constants was secured when we prepared the methyl-pentadiene hydrochloride with an excess of hydrogen chloride (a 10 g gain in weight per 17 g of the diene mixture); i.e., under conditions that promote an allyl rearrangement.

In later tests the hydrochloride of the 2- and 4-methylpentadiene-1,3 was prepared (with a yield of 81% of the theoretical) by adding a stoichiometric quantity of hydrogen chloride to the dienes.

Adding hydrogen bromide to the methylpentadiene mixture. The hydrogen bromide was first freed of any bromine and dried by passing it through a system of tubes containing red phosphorus on glass beads and calcined calcium chloride. Chilling with snow and salt was used for the reaction; the addition of the stoichiometric quantity of hydrogen bromide (15 g of hydrogen bromide to 15 g of the methylpentadiene mixture) was complete within 20-30 minutes, the reaction being slow at the start and proceeding at high velocity only after some time had elapsed. After the unreacted hydrogen bromide had been removed from the synthesized hydrobromide (85% of the theoretical yield) by passing anhydrous nitrogen through it at −70° and vacuum distillation, it possessed the following constants (this compound is not described in the literature):

B.p. 48.5-49.7° (30 mm); 26° (7 mm); n_D^{20} 1.4787; d_4^{20} 1.2077; MR_D 38.50; calculated 37.21, EM_D 1.29.

4.480 mg substance: 7.260 mg CO_2; 2.785 mg H_2O. 4.495 mg substance: 7.302 mg CO_2; 2.760 mg H_2O. 1.5972 mg substance: 0.6153 ml 0.02 N $AgNO_3$. 2.1860 mg substance: 0.6702 ml 0.02 N $AgNO_3$. Found %: C 44.22, 44.33; H 6.95, 6.87; Br 48.85; 49.00. $C_6H_{11}Br$: Calculated %: C 44.19; H 6.80, Br 49.00.

The hydrobromide proved to be wholly stable, its constant undergoing no change after repeated distillation or after standing for several days (at 4 or 5°).

Adding hydrogen bromide to individual 4-methylpentadiene-1,3 (VI) with a b.p. of 76.3° at 762 mm; n_D^{20} 1.4520 and d_4^{20} 0.7200, separated from the methylpentadiene mixture by treating the latter with maleic anhydride [14], yielded a hydrobromide with the same constants as those specified above:

B.p.53.5° (35 mm); 49.5° (30 mm); n_D^{20} 1.4795; d_4^{20} 1.2062.

Thus, 4-methylpentadiene-1,3 (VI) and a mixture of that hydrocarbon with the isomeric 2-methylpantadiene-1,3 (V) yield the same hydrobromide.

Reaction of ethylmagnesium bromide with the hydrochloride and hydrobromide of 2- and 4-methylpentadiene-1,3. A 1:1 ether solution of the hydrochloride (the hydrochloride was not distilled, but was placed in reaction immediately after its recovery from 20.5 g of the diene mixture) was chilled with dry ice and alcohol and then reacted with ethylmagnesium bromide (43.5 g of ethyl bromide and 9.8 g of magnesium), with constant stirring of the reaction mixture chilled to −20—30° (the molar proportions of the ethyl bromide, magnesium, and the hydrochloride being 1.5:1.6:1). After all the hydrochloride had been added (during the course of one hour), the reaction mass was stirred for another 2.5 hours at −20-−30° and then stirred 4-5 hours while being heated the next day. It was decomposed by pouring the reaction mixture over ice and adding acetic acid (15%).

After the customary treatment of the ether extract and the driving off of the ether, the reaction product was distilled with sodium into a column with an efficiency of 40 theoretical trays. All of it distilled within a narrow temperature range, its constants being as follows (the yield was 55% of the theoretical):

B.p. 107-107.3° (761 mm); n_D^{20} 1.4142; d_4^{20} 0.7210; MR_D 38.91; calculated 38.68.

The ethylmagnesium bromide was reacted with the hydrobromide secured from the 20.5 g of the methylpentadiene mixture in the same manner and using the same proportions as employed for the reaction of ethylmagnesium bromide with the hydrochloride, the only difference being that the hydrobromide was placed in the reaction with the reaction mixture chilled to a still lower temperature: down to −40–−50°.

The product of this reaction possessed exactly the same constants as those cited above, though its yield was higher—70% of the theoretical, based on the initial methylpentadiene mixture:

B.p. 107.2-107.4° at 756 mm; n_D^{20} 1.4146; d_4^{20} 0.7213.

3.800 mg substance: 11.925 mg CO_2; 4.888 mg H_2O. 3.785 mg substance: 11.899 mg CO_2; 4.830 mg H_2O. Found %: C 85.62, 85.74; H 14.39; 14.28: C_8H_{16}. Calculated %: C 85.62; H 14.38.

It should be noted that exactly the same results were obtained whether the hydrobromide was vacuum-distilled before the reaction or reacted directly after it had been prepared from the methylpentadiene mixture.

The constants of the collected hydrocarbon fraction were quite close to those of two possible reaction products: 4,4-dimethylhexene-2 (A) and 2,4-dimethylhexene-2 (B) (see Table).

		B.p.	n_D^{20}	d_4^{20}
Hydrocarbon fraction collected . . .		107.2-107.4° (756 mm)	1.4146	0.7213
4,4-Dimethylhexene-2 (A). .	[15] . .	105.4-106 (760 mm)	1.4120	0.7202
	[16] . .	106.3-106.7 (749 mm)	1.4155	0.7223
2,4-Dimethylhexene-2 (B). .	[17] . . .	108.9-109 (760 mm)	1.4144	0.7223

The Raman spectrum of the fraction with a b.p. of 107.2-107.4° contained only one frequency in the double-bond region: 1674 cm^{-1}. This frequency is typical of trisubstituted homologs of ethylene, such as 2,4-dimethylhexene-2 (B), as well as of the trans form of disubstituted ethylene homologs, such as 4,4-dimethylhexene-2 (A). Thus, 4,4-dimethylhexene-2 had a trans configuration; hence, we have to assign the same configuration to the tertiary hydrohalide (VII) of 4- and 2-methylpentadiene-1,3.

Bromination of the collected hydrocarbon fraction (6 g) was effected in a chilled chloroform solution. The reaction mixture was processed in the usual manner, the chloroform being driven off (at reduced pressure), and the bromination product fractionated in vacuum, yielding a dibromide (50% of the theoretical yield) that possessed the following constants:

B.p. 101-103° (10 mm), n_D^{20} 1.5113; d_4^{20} 1.4943; MR_D 54.56, calculated 54.67.

Figures in the literature for 4,4-dimethylhexene-2 dibromide (4,5-dibromo-3,3-dimethylhexane) [15]: b.p. 92-93° (4 mm); n_D^{20} 1.5113; d_4^{20} 1.5148; MR_D 54.21.

Hence, bromination yielded a stable dibromide as is typical of a symmetrical disubstituted homolog of ethylene, such as 4,4-dimethylhexene-2 (A) is. 2,4-Dimethylhexene-2 (B), a trisubstituted homolog of ethylene, ought to be converted by bromine into an unstable dibromide that evolves hydrogen bromide readily, giving rise to an unsaturated monobromide (as a matter of fact, a low-boiling fraction that darkened upon standing was driven off during the distillation of the bromination product).

To judge by the yield of the stable dibromide, the percentage of 4,4-dimethylhexene-2 (A) in the analyzed hydrocarbon fraction was at least 50%.

Oxidation of the hydrocarbon fraction (8 g) was effected with a 4% water—acetone (20% acetone) solution of permanganate in the cold, with vigorous stirring. The customary processing of the reaction mixture yielded 1.2 g of acetic acid with a b.p. of 117-120°, and dimethylacetic acid with a b.p. of 187-190° at 760 mm (no intermediate fraction was found).

According to A.E.Favorsky [18] dimethylethylacetic acid has a b.p. of 186-187.5° (755 mm). Analysis of the acid with a b.p. of 187-190° and of its silver salt indicated a composition that was that of dimethylethylacetic acid:

3.550 mg substance, 8.057 mg CO_2; 3.290 mg H_2O. 3,233 mg substance: 7.341 mg CO_2; 3.011 mg H_2O. Found %: C 61.90; 61.93; H 10.30, 10.35. $C_6H_{12}O_2$. Calculated %: C 62.07; H 10.35. 0,1000 g substance: 0.0481 g Ag. Found %: Ag 48.10. $C_6H_{11}O_2Ag$. Calculated %: Ag 48.37.

The acetic acid (the fraction with a b.p. of 117-120°) was identified by preparing acetanilide with a m.p. of 115° (after recrystallization); the mixed melting point exhibited no depression.

The production of acetic and dimethylethylacetic acids confirmed the presence of the 4,4-dimethylhexene-2, a hydrocarbon with a quaternary carbon atom (A), in the 107.2-107.4° hydrocarbon fraction.

The other possible constituent of this fraction — 2,4-dimethylhexene-2, a trisubstituted homolog of ethylene (B), is apparently oxidized by potassium permanganate more slowly than is 4,4-dimethylhexene-2, a disubstituted homolog of ethylene; therefore the absence in the oxidation products of methylethylacetic acid, which ought to appear as a result of oxidation of 2,4-dimethylhexene-2, cannot be regarded as evidence that this hydrocarbon is not present in the analyzed fraction. The presence of 2,4-dimethylhexene-2 in the fraction was proved by means of ozonidation.

Ozonidation of the hydrocarbon fraction (3 g) was effected in a chloroform solution. After the solvent had been driven off in vacuo, the ozonides were decomposed by prolonged heating with water; then the reaction mixture was heated with 2 ml of hydrogen peroxide, neutralized with soda, and distilled with steam. The distillate contained white crystals, consisting of acetone peroxide, with a m.p.of 131.5-132.5° (the literature [19] gives the m.p. as 132-133°). The production of acetone peroxide, the most typical product of the ozonidation of 2,4-dimethylhexene-2 (B), proved that the latter was present in the tested hydrocarbon fraction (the acids—acetic, methylethylacetic and dimethylethylacetic—were not isolated from the ozonidation products).

Thus, bromination, oxidation, and ozonidation combined to show that the product of the reaction of 4-methylpentadiene-1,3 (or 2-methylpentadiene-1,3) hydrobromide with ethylmagnesium bromide is a mixture of 4,4-dimethylhexene-2 (A) and 2,4-dimethylhexene-2 (B). The qualitative and quantitative composition of this mixture was finally established by hydrogenating it to a corresponding alkane mixture and then analyzing the latter optically.

Hydrogenation of the mixture of alkenes (50 g) was performed at 160-165° over platinized charcoal (15% (15% Pt).

Part of the catalysis product was distilled into a small dephlegmator for analysis of its Raman spectrum.1) In this analysis, chloroform was used as an internal standard.

Several Raman spectra of the test alkane mixture and of 2,4-dimethylhexane, to which a certain amount of chloroform was added, were photographed on the same plate. Blackening marks were placed on the plate, a photometric procedure [20] being employed to determine the ratio of the intensity of the line of the 2,4-dimethylhexane (B') selected for analysis to that of the 669 cm^{-1} line of chloroform in the spectra of the individual hydrocarbon and of the tested mixture of alkanes. (The 669 cm^{-1} chloroform line did not coincide with any other lines in the spectra, as had been determined by preliminary photographs.) The percentage of 2,4-dimethylhexane (B') was determined from its most intense line (827 cm^{-1}). Two independent, parallel determinations were made for other, less intense lines of this paraffin hydrocarbon, all these determinations yielding results that were close together. The Raman spectrum of the alkane mixture is given below;)2)

270(0); 318(3;b); 339(0.5); 358(0.8); 416(1.5;b); 441(1.8); 467(1); 500(0.6); **715-735(3;b)**; 767(1.5); 794(0.5); 815(1.2) **827(5)**; 857(1.2); 875(2); 907(3.5;b); 930(1); 956(4); 996(1.8); 1040-1050(2.5;b); 1085(1); 1100-1107(3;b); 1148(2); 1170(4); 1193(3); 1241(1.2); 1267 (1); 1309(1.8;b); 1344(1); 1382(1); 1443(10); 1463(9).

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1) We wish to express our gratitude to V.M.Tatevsky for his counsel concerning the optical analysis.

2) The intensities of the analytical lines, 827 cm^{-1} (for 2,4-dimethylhexane [21]) and 715-735 cm^{-1} (for 3,3-dimethylhexane [22]) in the spectrum of the tested mixture were determined photometrically; the intensities of the other lines were estimated visually; b denotes a wide band.

The concentration of 2,4-dimethylhexane by weight in the tested alkane mixture, $\underline{N_2}$, was determined from the formula:

$$N_2 = \frac{N_1 C_2}{C_1} \cdot \frac{\underline{I}_2}{I_2} \cdot \frac{\underline{I}_1}{I_1} \cdot \frac{1}{100 - C_2},$$

Where N_1 is the concentration of this hydrocarbon by weight in its mixture with chloroform; C_1 is the concentration of chloroform by weight in the same mixture; C_2 is the concentration of chloroform by weight in the chloroform solution of the alkane mixture, and $\underline{I}_1/I_1$ and $\underline{I}_2/I_2$, respectively, are the ratio of the intensity of analytical line 827 cm^{-1} for 2,4-dimethylhexane in its mixture with chloroform to that of the 669 cm^{-1} chloroform line, measured in the spectrum of the chloroform solution of 2,4-dimethylhexane, and in the spectrum of the chloroform solution of the test alkane mixture.

The optical analysis indicated that the alkane mixtures produced by hydrogenating the products of the reaction of ethylmagnesium bromide with the hydrobromide and the hydrochloride of the methylpentadienes have compositions that are very much alike; in the former case, the percentages of 2,4-dimethylhexane and 3,3-dimethylhexane were some 61 ±5% and some 39 ±5% respectively, the corresponding figures for the latter case being 58 ±5% and 42 ±5%.

Part of the resultant alkane mixture (32 g) was distilled with sodium into a column with an efficiency of 40 theoretical trays. The alkane mixture distilled throughout a wide temperature range (107-111°), in sharp contrast to the original mixture of alkenes, which distilled into the same column in a narrow range (107.2-107.4°). Refractionation (into a column with 60 theoretical trays) enabled us to separate the two components — 2,4-dimethylhexane (5 g) and 3,3-dimethylhexane (6 g), with an intermediate fraction totalling 17 g — in this alkane mixture (with a b.p. of 107-111°).

2,4-Dimethylhexane: b.p. 109° (768 mm); n_D^{20} 1.3960; d_4^{20} 0.7018; MR_D 39.11; calculated 39.14.
Literature data: b.p. 108.5-109° (740 mm); n_D^{20} 1.3967; d_4^{20} 0.7032 [23].

3,3-Dimethylhexane: b.p. 111-111.1° (768 mm); n_D^{20} 1.4005; d_4^{20} 0.7085; MR_D 39.13; calculated 39.14.
5.238 mg substance: 16.143 mg CO_2; 7.365 mg H_2O. 4.320 mg substance: 13.330 mg CO_2; 6.080 mg H_2O.
Found %. C 84.10, 84.21; H 15.73, 15.75. C_8H_{18}. Calculated %. C 84.12; H 15.88.
Literature data: b.p. 110.9° (754 mm); n_D^{20} 1.4014; d_4^{20} 0.7094 [24]; b.p. 110.7-111.2° (760 mm); n_D^{20} 1.3992; d_4^{20} 0.7078 [15].

Investigation of the Raman spectrum of the 3,3-dimethylhexane indicated that it contained no trace of 2,4-dimethylhexane.

Thus, about 40% of the hydrochloride and the hydrobromide of 2- or 4-methylpentadiene-1,3 reacts with ethylmagnesium bromide in their tertiary form, yielding an alkene with a quaternary carbon atom — trans-4,4-dimethylhexene-2, hydrogenation of which yields 3,3-dimethylhexane.

SUMMARY

1. Adding hydrogen chloride and bromide to 2- and 4-methylpentadiene-1,3 results in the formation of unsaturated tertiary halides of the allyl type that are unaffected by heating or distillation.

2. The hydrochloride and the hydrobromide of 2- and 4-methylpentadiene-1,3 (not described in the literature) react vigorously with ethylmagnesium bromide, yielding a mixture of two isomeric alkenes with adjacent boiling points: 4,4-dimethylhexene-2 and 2,4-dimethylhexene-2 (the yields being 55% and 70% of the theoretical, respectively). The formation of these two hydrocarbons is due to the fact that a tertiary hydrogen halide and an isomeric secondary hydrogen halide, related via an allyl rearrangement, take part in the reaction with the ethylmagnesium bromide.

3. The qualitative composition of the resultant alkene mixture was corroborated by the results of bromination, oxidation, ozonidation, and optical analysis. The quantitative composition of this mixture (some 40% of the hydrocarbon with a quaternary carbon atom — 4,4-dimethylhexene-2, and some 60% of the 2,4-dimethylhexene-2) was established by hydrogenating the mixture and analyzing the composition of the resulting alkane mixture by the Raman spectrum method.

4. It has thus been found that about 40% of the hydrochloride and the hydrobromide of 2- and 4-methylpentadiene-1,3 react with an organomagnesium bromide as tertiary allylic halides, which are characterized by having a methyl radical at the γ-position to the active halogen atom. In this respect the hydrohalides of 2- and 4-methylpentadiene-1,3 differ from the hydrohalides of isoprene and of 2,3-dimethylbutadiene-1,3, which react with organomagnesium compounds almost exclusively as primary allylic halides (only very slightly as tertiary halides).

5. It has been found (by the Raman spectrum method) that the 4,4-dimethylhexene-2 formed from the tertiary hydrohalide of 2- and 4-methylpentadiene-1,3 has a trans configuration, so that the initial unsaturated tertiary halide must possess the same configuration.

6. The high yield (70% of the theoretical) of the mixture of alkenes produced by reacting ethylmagnesium bromide with the hydrobromide of 2- and 4-methylpentadiene-1,3 and the substantial percentage of 4,4-dimethylhexene-2 (some 40%) in this mixture and of 3,3-dimethylhexane in the corresponding mixture of alkanes makes it possible to utilize the reaction studied in this paper for synthesizing alkanes with quaternary carbon atoms.

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Received June 16, 1950.

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[1] See Consultants Bureau English translation, p. 903.

[2] See Consultants Bureau English translation, p. 251.

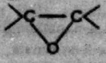
OXIDATIVE AND OXIDATIVE-HYDROLYTIC TRANSFORMATIONS OF ORGANIC MOLECULES

XX. THE STRUCTURE OF OXIDES OF UNSATURATED COMPOUNDS

M. M. Shemyakin, D. A. Bochvar, and L. A. Shchukina

As we have stated more than once [1-11], the oxides of various types of unsaturated compounds are substances that are frequently the end products in purely oxidative transformations of organic molecules, whereas these oxides occur as intermediate products in oxidative-hydrolytic reactions, which then undergo a series of subsequent changes.

It is natural that the structure and properties of oxides of unsaturated compounds are essential factors in a correct understanding of oxidative-hydrolytic transformations. Up to very recently the structure of compounds of this type has been represented by formulas of Type (I), which have been generally adopted. Some years ago, however, P. Karrer [12] asserted that the oxides of unsaturated compounds ought to be subdivided into two kinds: the first, not possessing an oxidizing ability and possessing a Type (I) structure, and the second, possessing oxidizing ability and a structure that was expressed by formulas of Type (II).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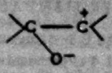
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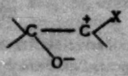
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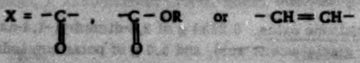

$$X = -\underset{\substack{\| \\ O}}{C}- \,,\quad -\underset{\substack{\| \\ O}}{C}-OR \quad \text{or} \quad -CH=CH-$$

P. Karrer emphasized that oxides of the first kind are characterized by an absence of substituents in their molecules that could polarize the C — O bond of the oxide group, while oxides of the second kind had such substituents. We know, as a matter of fact, that ethylene oxide, as well as its homologs and derivatives, which do not have strongly polarizing substituents immediately adjacent to the oxide group, have no oxidizing ability, whereas the oxides of α,β-unsaturated ketones and of some esters of α,β-unsaturated acids, as well as oxides of the carotenoids are oxidants [13].1) It is these comparisons that lead P. Karrer to the following conclusions:

1) When the oxide molecules have no polarizing substituents, their structure is expressed by Type (I) formulas, and their oxidic oxygen, connected by two covalent bonds to the carbon atoms, cannot possess oxidative ability.

2) When the oxide molecules contain substituents that can polarize the C — O bond of the oxide group, the structure of the oxides is represented by Type (II) formulas, or more accurately Type (III), so that they exhibit the properties of oxidants.

In our opinion P. Karrer's views are wrong, for the following reasons.

First, they are contradicted by certain arguments of a general nature. For, if we extend Karrer's standpoint consistently, the oxidative ability of oxides must be characterized quantitatively, say, by the values of the oxidative potentials determined under certain standard conditions. But then we will undoubtedly find a gradual transition from oxides with low oxidative ability to oxides with high oxidative ability, thus making any division of oxides into two kinds according to their oxidizing ability completely arbitrary.

Second, in expounding his views, P. Karrer ignores modern concepts of the nature of the polarizing action of the substituents he considers. In fact, he assigns Type (III) formulas to the oxides of α,β-unsaturated ketones and of esters of α,β-unsaturated acids, in these formulas the C — O bond of the oxide group being polarized in such a way as to produce a positive charge on the carbon atom linked to the carbonyl or carbalkoxy group. It is a matter of common knowledge, however, that a group of this sort can exert a polarizing effect, due to the shift of electrons only toward these groups. Hence, since P. Karrer ascribes a polarizing action to the carbonyl and carbalkoxy groups that is contrary to what is actually so, the Type (III) formulas proposed by him for these oxides are incorrect.

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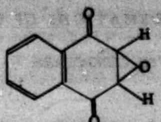
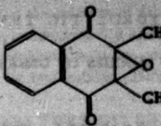
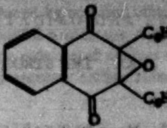
1) Oxides of α,β-unsaturated ketones and of esters of α,β-unsaturated acids, like the oxides of tertiary amines and iodoso compounds, oxidize monovalent negative iodine to free iodine.

Third, P. Karrer's views are contradicted by our experimental data on the oxidative ability of quinone oxides. On the basis of the concepts put forward by P. Karrer it should have been expected that such oxides as 1,4-naphthoquinone oxide, 2,3-dimethyl-1,4-naphthoquinone oxide, and 2,3-diphenyl-1,4-naphthoquinone oxide must not possess oxidative ability.







As a matter of fact, however, though the molecules of these oxides do possess carbonyl groups, the symmetrical structure of the molecules prevents these groups from affecting the degree of polarization of the C — O bonds of the oxide groups. Therefore, on the basis of P. Karrer's views, we should presuppose that all three of these oxides, which do not have structures represented by Type (II) formulas, will not exhibit any oxidative action. But 1,4-naphthoquinone oxide [10], 2,3-dimethyl-1,4-naphthoquinone oxide, and 2,3-diphenyl-1,4-naphthoquinone oxide (cf the experimental section below), as well as several other oxides of substituted p-benzo and p-naphthoquinones that we have investigated [3,10], do exhibit fairly well pronounced oxidative ability, readily oxidizing monovalent negative iodine to free iodine, for example, the oxides themselves being reduced to the respective quinones.

The foregoing compels us to conclude that P. Karrer's notions concerning the structure of oxides of unsaturated compounds are wrong.

EXPERIMENTAL

We have described the oxidative ability of the 2,3-oxides of 1,4-naphthoquinone, 2-methyl-1,4-naphthoquinone, 3-phenyl-1,4-naphthoquinone, potassium 2-methyl-1,4-naphthoquinone-3-sulfonate, and of 6-phenyl-1,4-benzoquinone in previous reports [3,10]. The results of our investigation of the oxidative ability of the 2,3-oxides of 2,3-dimethyl-1,4-naphthoquinone and of 2,3-diphenyl-1,4-naphthoquinone are set forth below.

1. Properties of 2,3-dimethyl-1,4-naphthoquinone oxide. 0.2284 g of 2,3-dimethyl-1,4-naphthoquinone oxide (m.p. 103-104° [14]) were dissolved in 45 ml of glacial acetic acid, and 5.0 g of potassium iodide was added to the solution. The solution (which was colored a light-brown even at room temperature by the iodine liberated) was boiled for 45 minutes, then cooled and diluted with 150 ml of water. The iodine liberated was back-titrated with a 0.1 N solution of hyposulfite, the amount of iodine being found to be 0.2774 g (96.6%, based on the initial oxide). After titration, the solution was extracted several times with ether, the ether solution being washed three times with a 10% aqueous solution of soda and then several times with water. The neutral ether solution was boiled with activated charcoal and dried with sodium sulfate. After the ether had been driven off, the yellow crystalline residue was dried to constant weight in vacuo at 80° and 5 mm. The melting point of the substance produced was 126°. A sample mixed with 2,3-dimethyl-1,4-naphthoquinone melted at the same temperature. The resultant quinone weighed 0.2056 g, this yield being 97.8%, based on the initial oxide.

2. Synthesis and properties of 2,3-diphenyl-1,4-naphthoquinone oxide. a) Synthesis of 2,3-diphenyl-1,4-naphthoquinone. 7 g of 2-phenyl-1,4-naphthoquinone, 105 ml of glacial acetic acid, and 8 g of benzoyl peroxide were heated to 115° for 2 hours 30 minutes. When the reaction was over, the solution was cooled and then poured into 300 ml of a saturated aqueous solution of sodium chloride. The yellow precipitate was filtered out, washed with water, and recrystallized from alcohol at first and then from glacial acetic acid. M.p. 139-140° [15]. Weight 2.3 g (25% yield).

b) Synthesis of 2,3-diphenyl-1,4-naphthoquinone oxide. 4.6 ml of 27% hydrogen peroxide was added to a hot solution of 2.1 g of 2,3-diphenyl-1,4-naphthoquinone in 50 ml of alcohol, followed by 11 ml of a 10% aqueous solution of soda. The solution was heated to a boil and then boiled for 7-8 minutes, after which it was cooled and poured into 200 ml of water. The precipitate was filtered out, washed with water, and recrystallized from alcohol containing activated charcoal. M.p. 155-156°. Weight 1.15 g; 52% yield.

Found %: C 80.81; H 4.36. $C_{22}H_{14}O_3$. Calculated %: C 80.98; H 4.29.

c) Properties of 2,3-diphenyl-1,4-naphthoquinone oxide. The oxidative properties of 2,3-diphenyl-1,4-naphthoquinone oxide were determined under the same conditions as those described above for 2,3-dimethyl-1,4-naphthoquinone oxide. The oxide sample weighed 0.2416 g; the iodine was found to total 0.1862 g (98.9%, based on the initial oxide). The ether solution yielded 0.2300 g of 2,3-diphenyl-1,4-naphthoquinone (m.p. 139-140°), or 100.1%, based on the initial oxide.

SUMMARY

It has been shown that the concepts put forward by P. Karrer concerning the structure of oxides of unsaturated compounds are wrong.

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Received June 30, 1950.

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3) " " " " " p. 419 ff.

4) " " " " " p.431 ff.

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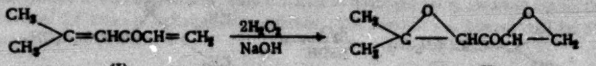
DERIVATIVES OF ACETYLENE. 132. α-KETONIC ETHERS AND THEIR TRANSFORMATIONS

III. THE MONOETHER OF β,β-DIMETHYL DIVINYL KETONE. OXIDATION OF VINYL ISOBUTYL KETONE AND ETHYL ISOBUTENYL KETONE WITH ALKALINE HYDROGEN PEROXIDE

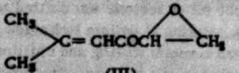
I. N. Nazarov and A. A Akhrem

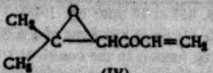
In our previous report we showed [1] that when β,β-dimethyl divinyl ketone (I) is oxidized with two moles of alkaline hydrogen peroxide a 60% yield of the corresponding ketonic diether (II) is obtained:


(I) (II)

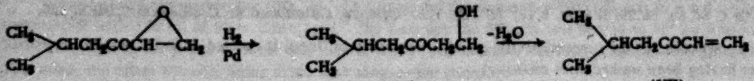
We were interested in making a study of the behavior toward alkaline hydrogen peroxide of the double bonds of β,β-dimethyl divinyl ketone (I), which possess differing degrees of substitution.

When β,β-dimethyl divinyl ketone (I) is oxidized with one molecule of alkaline hydrogen peroxide, it is principally the unsubstituted vinyl group that enters into reaction, giving rise to a 40% yield of the unsaturated monoether (III):

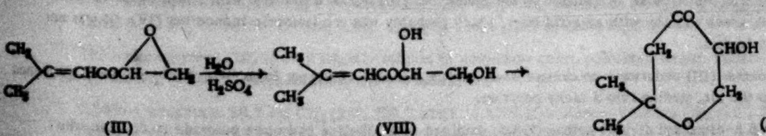

(III)


(IV)

Alongside the monoether (III), this reaction also yields the diether (II) and a small quantity of the isomeric monoether (IV), so that this reaction, in contrast to other addition reactions [2], is not rigidly selective. In contrast to the divinyl ketones, oxygen is added principally at the substituted double bond when ethylenic hydrocarbons are oxidized by acid hydroperoxides [3]. When the monoether (III) is partially hydrogenated (1 mole of H_2) in the presence of a palladium catalyst, it is chiefly the double bond that is hydrogenated, yielding the ketonic ether of vinyl isobutyl ketone (V). Exhaustive hydrogenation of the monoether (III) with a palladium catalyst results in rupture of the oxide ring, yielding the β-ketol (VI), which yields the previously described [4] vinyl isobutyl ketone (VII) when dehydrated with p-toluenesulfonic acid:

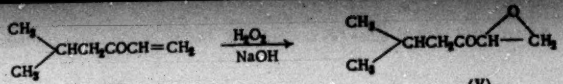

(V) (VI) (VII)

Hydrolysis of the monoether (III) with dilute sulfuric acid [5] yielded a crystalline product, 2,2-dimethyl-5-hydroxytetrahydro-4-pyrone (IX), which was formed by the cyclization of the intermediate unsaturated ketoglycol (VIII):


(III) (VIII) (IX)

The conversion of the unsaturated ketonic ether (III) into the hydroxypyrone (IX) by the action of dilute sulfuric acid is not a smooth reaction. In addition to the crystalline hydroxypyrone (IX), we get the ketoglycol (VIII) and an isomeric low-boiling product of unknown composition. Hydrolyzing the monoether (III) with water yielded the unsaturated ketoglycol (VIII).

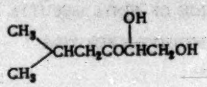
We also synthesized the saturated ketonic ether (V) by oxidizing vinyl isobutyl ketone (X) with alkaline hydrogen peroxide, the yield being 60%:

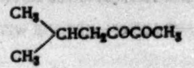


(X) (V)

Hydrolyzing the ketonic ether (V) with dilute sulfuric acid yielded the crystalline ketoglycol (XI):

(XI)

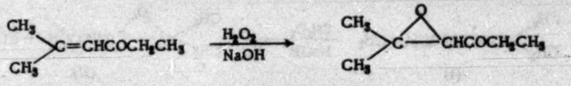




(XII)

The hydrolysis reaction was paralleled, however, by the isomerization of the ketonic ether (V) to the well-known α-diketone (XII) [5]. Hydrogenation of the ketonic ether (V) with a palladium catalyst yielded the β-ketol (VI) described above. As in the case of mesityl oxide [1], the oxidation of ethyl isobutyl ketone (XIII) with alkaline hydrogen peroxide is not a smooth reaction, a low yield of the ketonic ether (XIV) being produced:

(XIII)



(XIV)

In this reaction the formation of the ketonic ether (XIV) is paralleled by that of a high-boiling product with the empirical formula of $C_7H_{14}O_3$, an isomer of the ketoglycol.

EXPERIMENTAL

Preparation of the monoether of β,β-dimethyldivinyl ketone (III). A solution of 55 grams of β,β-dimethyl divinyl ketone (I) (b.p. 46° at 10 mm; n_D^{18} 1.4815) [4] in 500 ml of acetone was chilled to −10°, and 112 ml of 15% hydrogen peroxide (1 mole) and 8 ml of a 4 N aqueous solution of sodium hydroxide were added simultaneously from two dropping funnels in the course of 1 hour, with constant stirring and chilling. The solution temperature was kept at −10 to −6° by chilling the flask with a snow and salt mixture. One hour after the reagents had been added, the solution contained 1.13 g of hydrogen peroxide (17 g of hydrogen peroxide having been added). The alkali was neutralized with 10% sulfuric acid, the sodium sulfate was filtered out, pyrogallol was added, and the solvent was driven off in vacuo. The product was extracted with ether, dried with magnesium sulfate, and fractionated in vacuo after the ether had been driven off. This yielded 20 g of the monoether (III) as a colorless volatile liquid with a faint camphor odor.

B.p. 48.5-49° at 1 mm; n_D^{20} 1.4830; d_4^{20} 1.0247; MR_D 35.18; calculated 34.21.
8.680 mg substance: 21.16 mg CO_2; 6.24 mg H_2O. 10.950 mg substance: 26.60 mg CO_2; 7.98 mg H_2O.
0.1207 g substance; 12.0 g benzene: Δt 0.426°. 0.2829 g substance; 12.0 g benzene: Δt 0.967°.
Found %: C 66.49, 66.29; H 8.04, 8.15. M 123, 126. $C_7H_{10}O_2$. Calculated %: C 66.67; H 7.94; M 126.

The semicarbazone of the monoether (III) could not be recrystallized; it melted with decomposition at 132-133° after having been washed with methanol.

5.635 mg substance: 0.757 ml N_2 (22°, 752 mm). 7.473 mg substance: 1.021 ml N_2 (23°, 745 mm).
Found %: N 15.38, 15.45. $C_{15}H_{21}O_3N_3$. Calculated % N 14.43.

In another test, we secured, in addition to the monoether (III) 5 g of a fraction with a b.p. of 43-44° at 1.5 mm; n_D^{22} 1.4810, green in color with an acrid odor, which probably was the isomeric monoether (IV). It was not investigated any further.

The monoether (III) underwent no change when kept in a sealed container for a long time. It slowly thickened when exposed to the air, turning into a tacky polymer.

When the β,β-dimethyl divinyl ketone (I) was oxidized with alkaline hydrogen peroxide in dioxane, the yield of the monoether (III) dropped to 10%, about 10% of the previously described ketodiether (II) being produced, though the principal reaction product was a polymer.

Hydrogenation of the monoether (III). a) 6.3 g of the freshly distilled monoether (III) was dissolved in 40 ml of ethyl alcohol and hydrogenated with 0.1 g of a palladium catalyst on calcium carbonate. Hydrogenation set in immediately and continued at a rather high velocity, 1.28 liters of hydrogen being absorbed within 1 hour 15 minutes, after which hydrogenation was broken off. The coagulated catalyst was filtered out, the alcohol driven off, and the residue distilled in vacuo.

This yielded 1.8 g of the saturated ketonic ether (V) as a colorless, mobile liquid with a pleasant ethereal fragrance.

B.p. 67° at 12 mm; n_D^{20} 1.4340; d_4^{20} 0.9624 MR_D 34.57; calculated 34.68.
6.390 mg substance: 14.414 mg CO_2; 5.485 mg H_2O. 3.221 mg substance: 7.774 mg CO_2; 2.760 mg H_2O.
0.1408 g substance; 14.0 g benzene: Δt 0.392°. 0.3686 g substance; 14.0 g benzene: Δt 1.063°.
Found %: C 65.83, 65.86; H 9.60, 9.59. M 133, 128. $C_7H_{12}O_2$. Calculated %: C 65.63; H 9.37; M 128.

We were unable to recrystallize the semicarbazone of the ketonic ether (V). After it had been washed on the filter with methanol, it consisted of colorless crystals with a m.p. of 98° (decomp.).

3.350 mg substance: 0.677 ml N_2 (18°, 743 mm). 3.730 mg substance: 0.757 ml N_2 (21°, 742 mm).
Found %: N 22.82, 23.0. $C_8H_{15}O_2N_3$ Calculated %: N 22.70.

b) 8 grams of the monoether (III) was dissolved in 60 ml of ethyl alcohol and then hydrogenated for 7 hours with 0.15 g of a palladium catalyst. During the first hour and 15 minutes 2.5 liters of hydrogen was absorbed, after which hydrogenation slowed down considerably, only 0.1 liter of hydrogen being absorbed during the next 5 hours 45 minutes. A total of 2.6 liters of hydrogen was absorbed. The catalyst was filtered out, the alcohol driven off, and the product distilled in vacuo.

This yielded 2 grams of a fraction with a b.p. of 64.5-66° at 10 mm, corresponding to the ketonic ether (V) described above, plus 1.8 grams of a fraction of the β-ketol (VI) as a colorless liquid with a b.p. of 61° at 1 mm.

n_D^{20} 1.4352; d_4^{20} 0.9461; MR_D 35.87; calculated 36.06.

5.984 mg substance: 14.157 mg CO_2; 5.791 mg H_2O. 3.849 mg substance: 9.065 mg CO_2; 3.715 mg H_2O.
0.2167 g substance: 47.6 ml CH_4 (19°, 754 mm) by the Chugaev - Tserevitinov method.
Found %: C 64.56, 64.27; H 10.83, 10.80; OH 15, 29. $C_7H_{13}O(OH)$. Calculated %: C 64.62; H 10.77; OH 13.08.

It formed a dihydrazone with a m.p. of 145° (from ethyl alcohol) when reacted with 2,4-dinitrophenylhydrazine.

3.795 mg substance: 0.766 ml N_2 (23°, 755 mm). 3.800 mg substance: 0.777 ml N_2 (23°, 750 mm).
Found %: N 23.13, 23.27. $C_{19}H_{22}O_8N_8$. Calculated %: N 22.95.

Dehydration of the β-ketol (VI). 1.8 grams of the ketol (VI) was distilled in vacuo with 0.08 g of p-toluenesulfonic acid. About 1 gram of substance was distilled at 30° and 10 mm, which was dried and redistilled in vacuo, yielding about 0.2 g of vinyl isobutyl ketone (VII) (b.p. 29-30° at 10 mm; n_D^{18} 1.4280) a yellow liquid with an acrid odor and strong lachramatory effect [4].

When reacted with semicarbazide, this vinyl ketone yielded an addition product with a m.p. of 175-176° (from alcohol).

Hydrolysis of the monoether (III). a) 13.3 grams of the monoether (III) was left to stand overnight at room temperature with 130 ml of 3% sulfuric acid. The next day the mixture was heated to 70° for 8 hours and on a boiling water bath for 2 hours. A tar was seen to form. The solution was then saturated with potash and extracted with ether, the ether extracts being dried with magnesium sulfate.

One gram of crystals of the hydroxypyrone (IX) settled out of the anhydrous ether solution as minute, silky, white needles with a m.p. of 158° (from chloroform).

2.632 mg substance; 5.635 mg CO_2; 2.000 mg H_2O. 5.638 mg substance: 12.027 mg CO_2; 4.260 mg H_2O.
Found %: C 58.42, 58.21; H 8.50, 8.45. $C_7H_{12}O_3$. Calculated %: C 58.38; H 8.34.

The hydroxypyrone (IX) is very slightly soluble in anhydrous ether, petroleum ether, benzene, or dioxane, but freely soluble in water, ethyl alcohol, and methanol.

0.0486 g substance: 18.7 ml CH_4 (20°, 729.7 mm). 0.0662 g substance; 26.2 ml CH_4 (20°, 729.7 mm).
Found %: OH 25.32, 26.0. $C_7H_{10}O(OH)_2$. Calculated %: OH 23.60.

The hydroxypyrone (IX) forms no semicarbazone nor does it decolorize a chloroform solution of bromine (0°).

Driving off the ether yielded about 5 g of liquid hydrolysis products, which yielded 1 g of the ketoglycol (VIII) described above, with a b.p. of 97.5-98.5° at 1 mm; n_D^{19} 1.4965; and 2.5 g of a low-boiling product of unknown structure, with a b.p. of 57-58° at 1 mm; n_D^{21} 1.4624.

6.753 mg substance: 14.157 mg CO_2; 4.835 mg H_2O. 4.540 mg substance; 9.517 mg CO_2; 3.277 mg H_2O.
Found %: C 57.21, 57.21; H 8.01, 8.07. $C_7H_{12}O_3$. Calculated %: C 58.38; H 8.34.

b) A mixture of 5.3 g of the monoether (III) and 100 ml of distilled water (the two forming a stable emulsion) was heated on a boiling water bath for 7 hours. Driving off the water in vacuo yielded 3.5 g of a thick liquid, from which the unsaturated ketoglycol (VIII) was isolated as a thick, nearly colorless, odorless syrup with a b.p. of 103° at 2 mm by triple distillation.

n_D^{20} 1.4995; d_4^{20} 1.1081; MR_D 38.19; calculated 37.13.

7.165 mg substance: 15.158 mg CO_2; 5.350 mg H_2O. 7.244 mg substance: 15.373 mg CO_2; 5.516 mg H_2O. Found %: C 57.73, 57.91; H 8.35, 8.52. $C_7H_{12}O_3$. Calculated %: C 58.38; H 8.34.

The ketoglycol (VIII) rapidly decolorized a chloroform solution of bromine.

Oxidation of vinyl isobutyl ketone (X) by alkaline hydrogen peroxide. Synthesis of the ketonic ether (V). The vinyl isobutyl ketone employed in these experiments was prepared by splitting methanol out of 1-methoxy-5-methylhexan-3-one with p-toluenesulfonic acid as described earlier [7]; its constants were as follows: b.p. 41-42° at 22 mm; n_D^{15} 1.4293.

A solution of 95 g of vinyl isobutyl ketone (X) in 500 ml of dioxane was chilled to -6°, and 220 ml of a 15% solution of hydrogen peroxide (1 mole) and 10 ml of a 4 N aqueous solution of sodium hydroxide were added simultaneously from two dropping funnels during the course of 1 hour 20 minutes. Continuous stirring and chilling with a snow-salt mixture were used during the reaction. Considerable heat was evolved. After the reagents had been added, the reaction mixture contained 5 g of hydrogen peroxide (35 g of H_2O_2 having been added).

The residual hydrogen peroxide was decomposed with manganese dioxide, the alkali was neutralized with 10% sulfuric acid, the precipitated sodium sulfate was filtered out, the solvent was driven off in vacuo, and the products were extracted with ether, dried with sodium sulfate, and fractionated in vacuo. This yielded 69 g of a substance with a b.p. of 75-79° at 22 mm, further fractionation of which yielded 50 g of the ketonic ether (V) described above, as faintly odorous, colorless, mobile liquid with a b.p. of 77° at 22 mm; n_D^{20} 1.4303.

6.468 mg substance: 15.432 mg CO_2; 5.688 mg H_2O. 4.820 mg substance: 11.654 mg CO_2; 4.350 mg H_2O. Found %: C 65.11, 65.02; H 9.84, 9.95. $C_7H_{12}O_2$. Calculated %: C 65.63; H 9.37.

10 grams of this ketonic ether was dissolved in 40 ml of ethyl alcohol and hydrogenated with a palladium catalyst; 1.3 liters of hydrogen was absorbed during 10 hours, after which hydrogenation was stopped. This yielded 3 g of the β-ketol (VI) as a colorless liquid.

B.p. 73-73.5° at 4 mm; n_D^{20} 1.4318.

3.930 mg substance: 9.340 mg CO_2; 3.868 mg H_2O. 5.600 mg substance: 13.248 mg CO_2; 5.448 mg H_2O. Found %: C 64.85, 64.57; H 11.0, 10.89. $C_7H_{14}O_2$. Calculated %: C 64.62; H 10.77.

Reaction with 2,4-dinitrophenylhydrazine yielded a dihydrazone as yellow crystals with a m.p. of 124° (from alcohol).

4.035 mg substance: 1.029 ml N_2 (21°, 735 mm). 5.010 mg substance: 1.043 ml N_2 (22°, 736 mm). Found %: N 23.41, 23.33. $C_{19}H_{20}O_8N_8$. Calculated %: N 22.95.

Hydrolysis of the ketonic ether (V). 19.5 g of the ketonic ether (V) was boiled for 20 hours with 230 ml of 2% sulfuric acid. A layer of a brown liquid formed on the surface of the water. The oily layer was removed, and the solution was neutralized with sodium bicarbonate and evaporated in vacuo. The product was extracted with ether, dried with magnesium sulfate, and filtered, after which the ether was driven off.

4.718 mg substance: 9.926 mg CO_2; 4.042 mg H_2O. 4.829 mg substance; 10.172 mg CO_2; 4.060 mg H_2O. 0.0748 g substance: 27.7 ml CH_4 (24°, 756 mm) by the Chugaev-Tserevitinov method. 0.2235 g substance: 16.0 g dioxane: Δt 0.444°. 0.3238 g substance; 16.0 g dioxane: Δt 0.657°. Found %: C 57.41, 57.48; H 9.58, 9.41; OH 25.48. M 142, 145. $C_7H_{12}O(OH)_2$. Calculated %: C 57.53; H 9.59; OH 23.29; M 146.

3.5 grams of the thinnest silvery-white flakes of the ketonic glycol (XI) settled out of the ether solution; its m.p. was 71-72° after recrystallization from petroleum ether.

The semicarbazone of the ketoglycol (XI) was not found.

Recovery of the α-diketone (XII). The separated oily layer was dissolved in ether and dried with magnesium sulfate. The ether was driven off, the residue distilled in vacuo; yield 6 g of a substance with b.p. 46-48° at 20 mm.

Distillation at standard pressure yielded 5 g of the α-diketone (XII) as a mobile yellow liquid with b.p. 138-139°. n_D^{20} 1.4119; d_4^{20} 0.9135; MR_D 34.86. Calculated 34.55.

The α-diketone (XII) readily forms a dioxime: lustrous white leaflets with m.p. 172-173° (from dilute alcohol).

3.985 mg substance: 0.617 ml N_2 (25°, 744 mm). 4.005 mg substance: 0.632 ml N_2 (25°, 743 mm).
Found %: N 17.36, 17.67. $C_7H_{14}O_2N_2$. Calculated %: N 17.70.

The boiling point of the α-diketone (XII) is given as 138° in the literature [6], its dioxime fusing at 168°.

Oxidation of ethyl isobutenyl ketone (XIII) with alkaline hydrogen peroxide. The ethyl isobutenyl ketone employed in these experiments was prepared by partially hydrogenating β,β-dimethyl divinyl ketone as described previously [7]; its constants were as follows: 146-147°; n_D^{20} 1.4420.

4 g of ethyl isobutenyl ketone (XIII) was dissolved in 55 ml of methanol and chilled and continuously stirred while 9 ml of a 15% solution of hydrogen peroxide (1 mole) and 2.5 ml of a 4 N solution of sodium hydroxide were added simultaneously from two dropping funnels in the course of 15 minutes. Considerable heat was evolved. The reaction mass contained 0.4 g of hydrogen peroxide (1.35 g of hydrogen peroxide had been added initially) 45 minutes after the reagents had been added to the reaction mixture. The solution was neutralized with 10% sulfuric acid, the excess hydrogen peroxide was decomposed with manganese dioxide, the solution was diluted with twice its volume of water, and the products were extracted with ether. The ether extracts were dried with magnesium sulfate, the ether was driven off, and the residue was distilled in vacuo. This yielded a small amount of the ketonic ether (XIV) as a colorless liquid with b.p. of 77-78° at 21.5 mm; n_D^{20} 1.4315.

4.560 mg substance: 10.792 mg CO_2; 3.900 mg H_2O. 4.460 mg substance: 10.563 mg CO_2; 3.800 mg H_2O.
Found %: C 64.58, 64.63; H 9.57, 9.53. $C_7H_{12}O_2$. Calculated %: C 65.63; H 9.37.
The ketonic ether (XIV) does not form a semicarbazone.

In addition to the ketonic ether (XIV), this experiment also yielded a small quantity of a substance with b.p. 63° at 4 mm; n_D^{21} 1.4365, which was, probably, a compound that was isomeric with the ketoglycol as had been the case in the oxidation of mesityl oxide [1].

9.80 mg substance: 21.12 mg CO_2; 8.51 mg H_2O. 20.49 mg substance: 44.18 mg CO_2; 17.35 mg H_2O.
Found %: C 58.61, 58.84; H 9.71, 9.60. $C_7H_{14}O_3$. Calculated %: C 57.53; H 9.59.

This product was not investigated any further.

SUMMARY

When one molecule of alkaline hydrogen peroxide is reacted with β,β-dimethyl divinyl ketone (I), the oxygen is added chiefly at the unsubstituted vinyl group, producing a 40% yield of the unsaturated monoether (III). Hydrogenation of the monoether (III) yields the saturated ketonic ether (V), which was also synthesized, with a yield of 60%, by oxidizing vinyl isobutyl ketone with alkaline hydrogen peroxide.

Exhaustive hydrogenation of the monoether (III) with a palladium catalyst ruptures the oxide ring and yields the β-ketol (VI), which was also synthesized by hydrogenation of the ketonic ether (V). Hydrolyzing the unsaturated monoether (III) with 3% sulfuric acid yields 2,2-dimethyl-5-hydroxytetrahydro-4-pyrone (IX), while hydrolysis with water yields the unsaturated ketoglycol (VIII). When the ketonic ether (V) is heated with 2% sulfuric acid, the normal hydrolysis reaction and the formation of the ketoglycol (XI) are paralleled by the isomerization of the ketonic ether (V) to the well-known α-diketone (XII). As in the case of mesityl oxide, the oxidation of ethyl isobutenyl ketone (XIII) with alkaline hydrogen peroxide is a less smooth reaction, a low yield of the ketonic ether (XIV) being produced.

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Received June 2, 1950.

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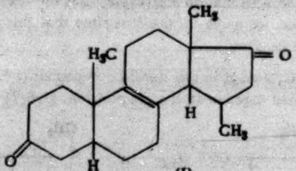
DERIVATIVES OF ACETYLENE

133. SYNTHESIS OF POLYCYCLIC COMPOUNDS RELATED TO THE STEROIDS

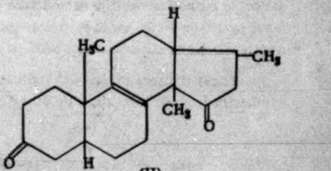
X. THE DIENE CONDENSATION OF 2-METHOXY-1,3-BUTADIENE WITH Δ^1- CYCLOHEXEN-6-ONE

I. N. Nazarov and L. D. Bergelson

In one of our preceding reports [1] we described the diene condensation of 2-methoxy-1,3-butadiene with 1-methyl-Δ^1-cyclohexen-6-one, which resulted in the complete synthesis of the stereoisomer (I) or of the structural iosmer (II) of $\Delta^{8,9}$-15-methylandrostene-3,17-dione:

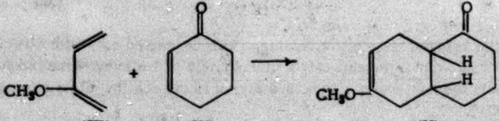


(I)



(II)

We were interested in effecting a similar condensation of 2-methoxybutadiene (III) with Δ^1 - cyclohexen-6-one (IV) since the resultant cis-6-methoxyoctalone (V) is not only a model compound enabling one to study the stereochemical behavior patterns of diene condensation, but might also serve as an intermediate in the synthesizing of norsteroid compounds with cis and trans configurations of the A/B rings.



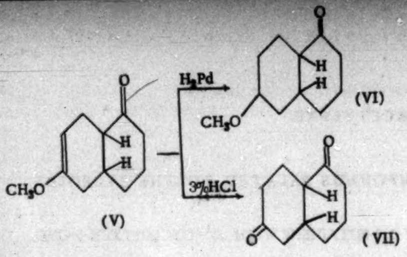
(III) (IV) (V)

Like the condensations with other α,β-unsaturated cyclic ketones, a satisfactory yield can be obtained in the condensation of the methoxybutadiene (III) with Δ^1-cyclohexen-6-one (IV) only at 190-200° in a solution containing a large excess of the ketone, since the predominant reaction is the dimerization of the methoxybutadiene when the conditions are milder or the dilution is insufficient. It is also advisable to carry out the reaction in an atmosphere of nitrogen or carbon dioxide with antioxidants present. Under these conditions the yield of 6-methoxyoctalone (V) may be made as high as 15-20% , based on the reacted cyclohexenone.

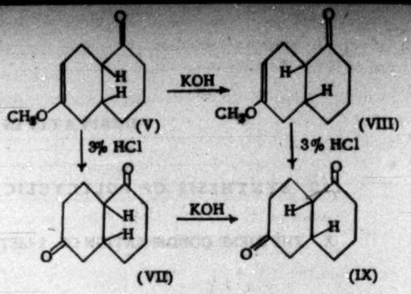
As with other enolic ethers, methoxyoctalone (V) is hydrogenated in ether only when a Pd catalyst is present, being converted then into 6-methoxydecalone (VI). Hydrolysis of the cis-methoxyoctalone (V) with dilute solutions of mineral acids produces a nearly quantitative yield, even in the cold, of the crystalline cis-1,6-diketodecalin (VII) (see Scheme A on following page).

The action of an alkali upon cis-methoxyoctalone (V) readily isomerizes it to trans-methoxyoctalone (VIII), which is hydrolyzed by dilute mineral acids to the high-melting trans-1,6-diketodecalin (IX). This same diketone may be prepared from the low-melting cis-1,6-diketodecalin (VII) by heating the latter with an alcoholic alkali (see Scheme B on following page).

The rules established by Huckel [2] for the α - decalone series indicate that the low-melting diketodecalin (VII) and the corresponding methoxyoctalone (V), as well as the methoxydecalone (VI), must have cis configurations.



Scheme A

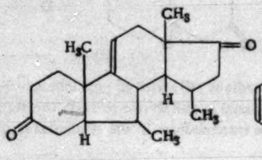


Scheme B

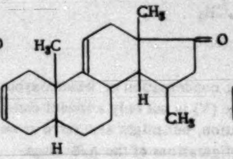
The high melting diketone (IX) and methoxyoctalone (VIII) must, accordingly, be trans isomers. It is worthy of note that the isomeric 1,6-diketodecalins (VII) and (IX) yield the same disemicarbazone of the trans isomer. An analogous phenomenon has been observed in similar cases [2,3,4].

In 1937 Alder and Stein [5] advanced the hypothesis, on the basis of their investigation of the diene condensation of butadiene with benzoquinone and of cyclopentadiene with maleic anhydride, that the diene synthesis always results in a cis addition compound. In the present paper, we prove for the first time that this postulate also applies to diene condensations with α,β-unsaturated cyclic ketones.

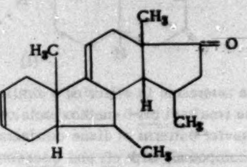
These findings of ours also indicate that the A/B and C/D rings in the steroid compounds (I, X, XI, and XII) synthesized in our laboratory by diene condensations are joined together in the cis position [1,6,7]:



(X)

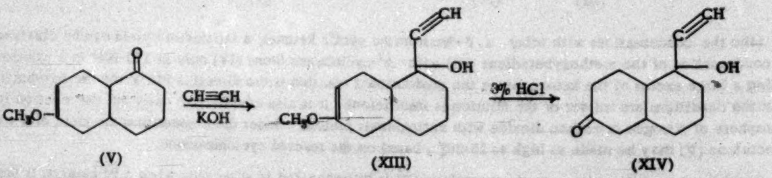


(XI)



(XII)

In contrast to other cyclic ketones, the methoxyoctalone (V) is condensed only with difficulty with acetylene when powdered potassium hydroxide is present, only a minute yield of 1-ethynyl-6-methoxyoctalol (XIII) being obtained. This acetylenic methoxyoctalol can be hydrolyzed in the cold by dilute mineral acids, yielding the acetylenic ketodecalol (XIV).



We propose to utilize the acetylenic alcohols (XIII) and (XIV) to synthesize compounds with the skeleton of 10-norandrostane.

EXPERIMENTAL

Diene condensation of 2-methoxy-1,3-butadiene with Δ^1-cyclohexen-6-one. These experiments were performed in a metallic ampoule in an atmosphere of nitrogen or carbon dioxide. Vacuum fractionation was performed in a current of anhydrous air.

a) 86 g of the Δ^1-cyclohexenone was heated with 28 g of 2-methoxybutadiene to 190-200° for 5 hours. Fractionation yielded 55 g of the initial cyclohexenone, 7.3 g of the dimer of 2-methoxybutadiene [8], and 16 g of condensation products with a b.p. of 120-139° at 4 mm. Refractionation of the last fraction yielded 8.5 g of

Δ^6-*cis*-6-methoxy-1-octalone (V) as a viscous yellow oil with a faint camphor odor, a b.p. of 96-98° at 0.1 mm, and of 129.5-132° at 4 mm; n_D^{20} 1.5063.

b) 35 g of the Δ^1-cyclohexenone was heated to 185-190° for 25 hours with 10 g of 2-methoxybutadiene in 15 ml of absolute dioxane. Fractionation yielded 30 g of the initial cyclohexenone, 3.5 g of the dimer of the methoxybutadiene, and 2.8 g of the methoxyoctalone (V) with a b.p. of 128-132° at 4.5 mm; n_D^{20} 1.5040.

Analysis of the Δ^6-cis-6-methoxy-1-octalone (V) (from Experiment *a*):
7.875 mg substance: 21.228 mg CO_2; 6.097 mg H_2O. 4.575 mg substance: 12.297 mg CO_2; 3.540 mg H_2O.
Found %: C 73.5, 73.3; H 8.7, 8.7. $C_{11}H_{16}O_2$. Calculated %: C 73.3; H 8.9.

When the methoxyoctalone was reacted with semicarbazide acetate in absolute methanol, the water evolved saponified the vinyl ether, the monosemicarbazone of *trans*-1,6-diketodecalin (IX), m.p. 227° (from alcohol) settling out.

3.560 mg substance: 0.584 ml N_2 (20°, 749 mm). 3.210 mg substance: 0.523 ml N_2 (20°, 748 mm).
Found %: N 18.8, 18.7: $C_{11}H_{17}O_2N_3$. Calculated %: N 18.8.

Hydrogenation of cis-Δ^6-6-methoxy-1-octalone (V). 2.4 g of the 6-methoxyoctalone was hydrogenated in absolute ether with a Pd catalyst, 245 ml of hydrogen being absorbed in 8 hours (280 ml called for theoretically). Fractionation yielded 2.1 g of *cis*-6-methoxy-1-decalone (VI); b.p. 124° at 5 mm; n_D^{20} 1.4987.

5.878 mg substance: 15.700 mg CO_2; 5.257 mg H_2O. 5.112 mg substance: 13.650 mg CO_2; 4.565 mg H_2O.
Found %: C 72.9, 72.8; H 10.0, 10.0. $C_{11}H_{18}O_2$. Calculated %: C 72.5; H 10.0.

Practically no hydrogen was absorbed when the 6-methoxyoctalone (V) was hydrogenated in ethyl alcohol with a Pd catalyst.

Hydrolysis of cis-Δ^6-6-methoxy-1-octalone (V). 5 g of the methoxyoctalone (V) was agitated for 3 hours at room temperature with 20 ml of 3% hydrochloric acid. The mixture was then saturated with ammonium chloride the organic layer being removed, the aqueous layer extracted with ether, and the combined ether solutions neutralized with a 5% soda solution and dried with magnesium sulfate. Driving off the ether left behind a solid mass. Recrystallization from benzene yielded 3.9 g of *cis*-1,6-diketodecalin (VII) as colorless lamellar crystals with a m.p. of 87-88°.

3.710 mg substance: 9.812 mg CO_2; 2.820 mg H_2O. 6.698 mg substance: 17.662 mg CO_2; 5.090 mg H_2O.
Found %: C 72.2, 72.0; H 8.5, 8.5. $C_{10}H_{14}O_2$. Calculated %: C 72.3; H 8.5.

The disemicarbazone of the synthesized diketone was insoluble in organic solvents. After having been washed repeatedly with ether and alcohol it fused with decomposition at 243-244° (in a sealed capillary).

3.180 mg substance: 0.828 ml N_2 (19°, 744 mm). 3.750 mg substance: 0.982 ml N_2 (21°, 749 mm).
Found %: N 29.8, 30.0. $C_{12}H_{20}O_2N_6$. Calculated %: N 30.0.

Isomerization of cis-1,6-diketodecalin (VII). 0.4 g of *cis*-1,6-diketodecalin (m.p. 87°) was heated to a boil with 35 ml of 10% alcoholic alkali for 3 hours. Most of the alcohol was driven off, and the residue diluted with water and extracted with ether, the ether extract being neutralized with acetic acid and dried with magnesium sulfate. Driving off the ether left behind 0.25 g of the acicular crystals of *trans*-1,6-diketodecalin (IX), which had a m.p. of 125-126° after recrystallization from benzene.

4.300 mg substance: 11.380 mg CO_2; 3.320 mg H_2O. 5.290 mg substance: 14.050 mg CO_2; 4.100 mg H_2O.
Found %: C 72.2, 72.4; H 8.6, 8.6. $C_{10}H_{14}O_2$. Calculated %: C 72.3; H 8.5.

The disemicarbazone of *trans*-1,6-diketodecalin (IX) fused at 243° with decomposition. The mixed melting point with the disemicarbazone prepared from the *cis*-diketodecalin (VII) showed no depression.

Isomerization of cis-Δ^6-6-methoxy-1-octalone (V). Trans-Δ^6-6-methoxy-1-octalone (VIII) was recovered in one of our attempts to condense the *cis*-methoxyoctalone (V) with acetylene in the presence of powdered potassium hydroxide.

8 grams of the *cis*-methoxyoctalone (V) was placed in 40 ml of absolute ether, and 4 g of powdered potassium hydroxide and 80 ml of ether, previously chilled to -15° and saturated with acetylene, were added drop by drop in a current of acetylene during the space of one hour and a half. Acetylene was passed through for another hour and a half with chilling and stirring, and then for two more hours at room temperature. 10 ml of water was added to the mixture, the ether was separated, the aqueous layer extracted with ether, and the combined ether solutions

neutralized by passing carbon dioxide through and then dried with potash. Fractionation yielded 5.4 g of trans-Δ^6-6-methoxy-1-octalone (VIII), with a b.p. of 123° at 4.5 mm; n_D^{20} 1.5010.

4.130 mg substance: 11.112 mg CO_2; 3.225 mg H_2O. 5.177 mg substance: 13.895 mg CO_2; 4.020 mg H_2O. Found %: C 73.4, 73.3; H 8.7, 8.7. $C_{11}H_{16}O_2$. Calculated %: C 73.3; H 8.9.

5 grams of the trans-6-methoxy-1-octalone was agitated for 3 hours with 20 ml of 3% hydrochloric acid. Then the mixture was saturated with ammonium chloride and extracted with ether, and the ether solution neutralized with a 5% soda solution and dried with magnesium sulfate. Driving off the ether left behind 4.2 g of colorless crystals that fused at 124-125° (from benzene). The mixed melting point with trans-1,6-diketodecalin exhibited no depression.

Condensation of cis-Δ^6-6-methoxy-1-octalone (V) with acetylene. A solution of 3 g of the cis-6-methoxy-octalone (V) in 10 ml of absolute ether was added, with vigorous stirring, in a current of acetylene during the course of 2 hours to a mixture of 2.3 g of powdered potassium hydroxide and 20 ml of ether that had been previously chilled to −15° and saturated with anhydrous acetylene. The acetylene was then passed through for 2 hours while the mixture was chilled, and for 12 hours the next day at room temperature. 10 ml of water was added to the solidified mixture, the ether layer was separated, the aqueous layer extracted with ether, and the combined ether solutions neutralized by passing through carbon dioxide, dried with potash, and vacuum-fractionated in a current of anhydrous nitrogen. This yielded 1.0 g of 1-ethynyl-6-methoxy-1-octalol (XIII) (b.p. 112-115° at 0.05 mm) as a thick colorless mass that slowly crystallized upon standing and yielded a white precipitate with ammoniacal silver nitrate. After recrystallization from petroleum ether the crystals had a m.p. of 62-64.5°, the m.p. rising to 69-71° after drying in vacuo over phosphoric anhydride (they totaled 0.6 g).

4.310 mg substance: 11.947 mg CO_2; 3.510 mg H_2O. 5.880 mg substance: 16.240 mg CO_2; 4.790 mg H_2O. Found %: C 75.6, 75.4; H 9.1, 9.1. $C_{13}H_{18}O_2$. Calculated %: C 75.7; H 8.8.

Hydrolysis of Δ^6-1-ethynyl-6-methoxy-1-octalol (XIII). The mother liquor left after the recrystallization of the acetylenic alcohol (XIII) was agitated for 3 hours at room temperature with 10 ml of 3% hydrochloric acid. The mixture was then saturated with ammonium chloride and extracted with ether, the ether layer being neutralized with a 5% soda solution and dried with magnesium sulfate. After the ether had been driven off, a solution of semicarbazide acetate in methanol (a threefold excess) was added to the residue. The semicarbazone that settled out after 15 days was separated in a soluble fraction and a fraction that was insoluble in hot methanol. The methanol-insoluble crystals fused at 239-241° in a sealed capillary (with decomposition), their mixed melting point with the disemicarbazone of the 1,6-diketodecalin exhibiting no depression. The crystals of the soluble fraction, which had a m.p. of 251-253° (with decomposition) after recrystallization from alcohol, were the semicarbazone of 1-ethynyl-6-ketodecalol (XIV).

3.200 mg substance: 0.478 ml N_2 (20°, 740 mm). 3.200 mg substance: 0.473 ml N_2 (19°, 740 mm). Found %: N 17.0, 16.8. $C_{13}H_{19}O_2N_3$. Calculated %: N 16.9.

SUMMARY

1. Δ^6-6-Methoxy-1-octalone (V), an intermediate product in the preparation of steroid compounds with the skeleton of 10-norandrostane, has been synthesized.

2. It has been shown that the diene condensations with α,β-unsaturated ketones result in cis addition compounds.

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Received June 2, 1950

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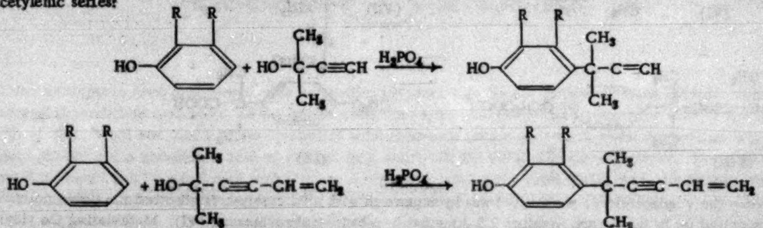
DERIVATIVES OF ACETYLENE

134. THE CONDENSATION OF TETRAMETHYLBUTYNEDIOL AND 2,5-DIMETHYL-1-5-HEXADIEN-3-YNE WITH PHENOL IN THE PRESENCE OF PHOSPHORIC ACID

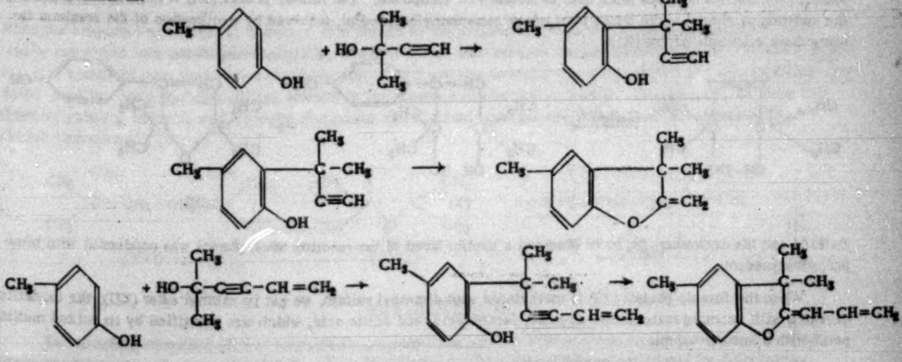
I. N. Nazarov and A. I. Kakhniashvili

The condensation of phenol and of the cresols with acetylenic and vinyl acetylenic alcohols was investigated for the first time by I. N. Nazarov and his associates [1]. The condensation was effected in the presence of phosphoric acid, producing a yield of some 50% of para-substituted phenols and cresols of the acetylenic and vinylacetylenic series:



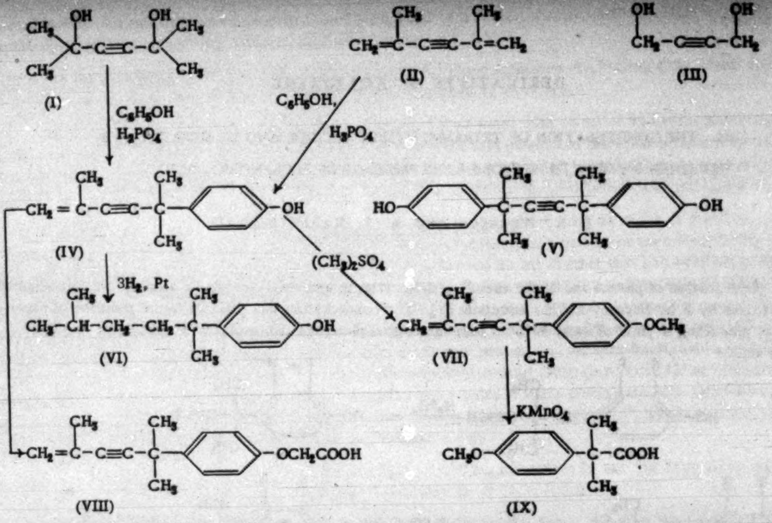
R = H or CH_3.

The same products are secured by condensing phenol and the cresols with the respective unsaturated hydrocarbons produced by dehydrating the acetylenic and vinylacetylenic alcohols. The condensation of acetylenic and vinylacetylenic alcohols with p-cresol results in the formation of an intermediate ortho-substituted cresol of acetylenic or vinylacetylenic structure, which is cyclized completely to methylene- or allylidenecoumarans under the reaction conditions.

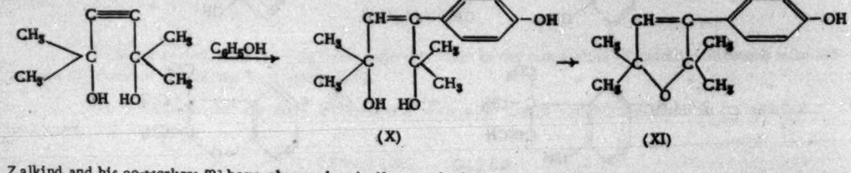


We were also interested in investigating the condensation of phenols with acetylenic glycols, and we used for this purpose the simplest representatives of primary and tertiary acetylenic γ-glycols – tetramethylbutynediol (I) and 2-butyne-1,4-diol (III).

Condensing phenol with tetramethylbutynediol (I) at 45-50° in the presence of phosphoric acid yielded two phenolic products, which proved to be 2,5-dimethyl-5-p-hydroxyphenyl-1-hexen-3-yne (IV) and 2,2,5,5-tetramethyl-3-p-hydroxyphenyl-Δ^3-dihydrofuran (XI):

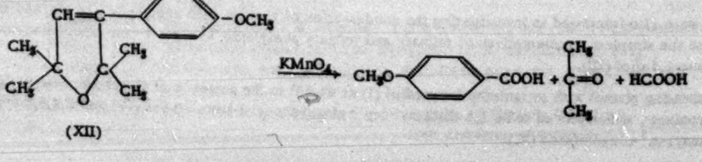


When the vinylacetylenic phenol (IV) was hydrogenated with a Pd catalyst, it absorbed the three molecules of hydrogen called for by the theory, yielding 2,5-dimethyl-5- p-hydroxyphenylhexane (VI). Methylating the vinylacetylenic phenol (IV) with dimethylsulfate yielded its methyl ester (VII), while reacting the vinylacetylenic phenol (IV) with chloroacetic acid yielded the corresponding crystalline phenoxyacetic acid (VIII). The structure of the vinylacetylenic phenol (IV) was conclusively proved by oxidizing its methyl ester (VII) with permanganate. This yielded, in addition to formic and acetic acids, a high yield of dimethyl-p-methoxyphenylacetic acid (IX), whose mixed melting point with a known sample exhibited no depression. It might have been thought that the condensing of phenol with tetramethylbutynediol would yield an acetylenic diphenol (V) in addition to the vinylacetylenic phenol (IV), but we have not been able to isolate that compound. The furanic phenol (XI) is most likely formed by the addition of phenol at the triple bond of the tetramethylbutynediol, followed by cyclization of the resultant intermediate ethylenic glycol (X):



Zalkind and his co-workers [2] have observed a similar trend of the reaction when phenol was condensed with tetraphenylbutynediol.

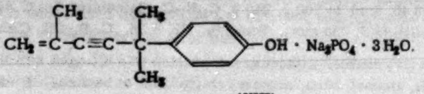
When the furanic phenol (XI) is methylated with dimethyl sulfate, we get its methyl ester (XII), the oxidation of which with permanganate yields acetone, formic acid, and anisic acid, which was identified by its mixed melting point with a known sample:



When phenol was condensed with 2,5-dimethyl-1,5-hexadien-3-yne (II) under the conditions specified above, all we got was the vinylacetylenic phenol (IV), none of the furanic phenol (XI) being formed, which bears out the mechanism proposed above for its formation. Nor were we able to secure the acetylenic diphenol (V) during this condensation, which might have been formed by the condensation of the dienyne (II) with two molecules of phenol.

Thus, the condensation of phenol with tetramethylbutynediol (I) in the presence of phosphoric acid follows two lines: 1) dehydration of the acetylenic glycol (I) to a dienyne (II), followed by condensation of this dienyne with phenol into the para-substituted vinylacetylenic phenol (IV); and 2) the addition of phenol at the triple bond of the acetylenic glycol (I) followed by cyclization of the ethylenic glycol (X) to the furan compound (XI). The first reaction line, resulting in formation of the vinylacetylenic phenol (IV), predominates.

We have secured a crystalline phosphorus-containing product (XIII)(m.p. 137-139°) from the alkaline extracts of the condensation products of phenol with the acetylenic glycol (I) and with the dienyne (II), the analysis of this product indicating that it was a double compound of sodium phosphate hydrate with the vinylacetylenic phenol (IV):

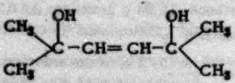


$CH_2=C(CH_3)-C\equiv C-C(CH_3)_2-C_6H_4-OH \cdot Na_3PO_4 \cdot 3H_2O.$

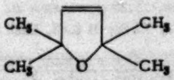
(XIII)

All our attempts to condense phenol with butynediol (III) met with failure, notwithstanding the wide range of experimental conditions employed. When gentle conditions were used (45-50° and phosphoric acid with a sp. gr. of 1.7), all the phenol and much of the butynediol were recovered unchanged, while when the conditions used were severe (60-80° and a phosphoric acid of 1.82 sp. gr.), nearly all the butynediol turned into tar. These results indicate that phenol can be condensed with tertiary acetylenic glycol much more easily than with primary compounds, as has also been observed in the condensation of phenols with saturated alcohols and glycols.

Lastly, we tried to condense phenol with tetramethylbutenediol (XIV) and tetramethyldihydrofuran (XV), but no condensation products at all were obtained.

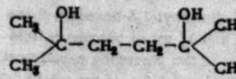


(XIV)

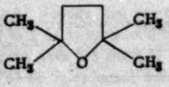


(XV)

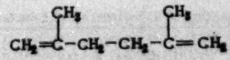
When the ethylenic glycol (XIV) is heated with phenol in the presence of an acid (phosphoric or sulfuric), it is readily converted into the dihydrofuran (XV), which is either recovered unchanged or turns into tar. In this connection, it is worthy of note that tetramethylbutanediol (XVI) and the corresponding furan (XVII) and diene (XVIII) condense readily with benzene and the phenols in the presence of aluminum chloride, sulfuric acid, or boron trifluoride, yielding bicyclic and tricyclic compounds (methylated tetralins and indans, and the corresponding phenolic compounds) [3].



(XVI)



(XVII)



(XVIII)

EXPERIMENTAL

Tetramethylbutynediol (I) was prepared by condensing acetylene with acetone in the presence of powdered potassium hydroxide; its m.p. was 92-94°. The 2,5-dimethyl-1,5-hexadien-3-yne was prepared by dehydrating tetramethylbutynediol with p-toluenesulfonic acid; its b.p. was 124-126°; n_D^{20} 1.4874.

Condensation of tetramethylbutynediol with phenol in the presence of phosphoric acid. 71 g of tetramethylbutynediol (I) was gradually added at 50°, with continuous stirring, to a mixture of 47 g of freshly distilled phenol and 26 ml of phosphoric acid (sp. gr. 1.704). The mixture was stirred at 45-55° for 15 hours. After it cooled, the product was extracted with ether, the ether extract being washed with water and then several times with a 10% solution of sodium hydroxide to extract the acid reaction products. The alkaline extracts were combined and acidulated with dilute hydrochloric acid, and the product was extracted with ether. The ether solution was dried with potash, and after the ether had been driven off, the residual acid products were distilled in vacuo in an atmosphere of nitrogen. This yielded 18 g of the unreacted phenol (b.p. 62-68° at 4 mm), 22 g of the substituted vinylacetylenic phenol (IV) (b.p. 132-138° at 4 mm; n_D^{20} 1.5505), and 10 g of the furanic phenol (XI) (b.p. 152-162° at 3 mm; n_D^{20} 1.5456). The polymer residue left after fractionation of the acid products totaled 22 g.

Fractionation of the ether solution containing the neutral products yielded 2 g of 2,5-dimethyl-1,5-hexadien-3-yne, (II), with a b.p. of 44-48° at 43 mm and 123-124° at atmospheric pressure; n_D^{20} 1.4872. We also secured 2.7 g of a mixture of high-boiling neutral products (b.p. 72-150° at 6 mm), which was not analyzed further. The polymer residue left after fractionation of the neutral products totaled 10 g.

Analysis of the vinylacetylenic phenol (IV). After the vinylacetylenic phenol (IV) had been refractionated it was a yellowish liquid with a b.p. of 126-129° at 2 mm;

n_D^{20} 1.548; d_4^{20} 0.9956; MR_D 63.8; calculated 62.32.

6.500 mg substance: 19.942 mg CO_2; 4.880 mg H_2O. 5.810 mg substance; 17.754 mg CO_2; 4.411 mg H_2O.
0.1866 g substance; 22.28 g benzene: Δt 0.213°. 0.2162 g substance; 22.28 g benzene: Δt 0.233°.
Found %: C 83.72, 83.5; H 8.40, 8.49; M 200.5, 210.4. $C_{14}H_{16}O$. Calculated %: C 84.0; H 8.0; M 200.
0.0829 g substance: 12 ml CH_4 (21°, 730 mm). Found %: OH 8.36. $C_{14}H_{15}OH$. Calculated %: OH 8.5.

The vinylacetylenic phenol (IV) distilled without decomposition in a nitrogen atmosphere and dissolved in a 10% solution of sodium hydroxide, alcohol, ether, acetone, chloroform, or benzene. It did not react with ferric chloride in either an aqueous or an alcoholic medium.

Analysis of the furanic phenol (XI): The fraction with a b.p. of 152-162° at 3 mm began to crystallize within a few days. Recrystallization of the product from ligroin yielded white crystals of the furanic phenol (XI) with a m.p. of 76-77°, which were soluble in alcohol, ether, petroleum ether, chloroform, and alkali.

4.230 mg substance: 11.979 mg CO_2; 3.316 mg H_2O. 4.012 mg substance: 11.358 mg CO_2; 3.081 mg H_2O.
Found %: C 77.3, 77.26; H 8.77, 8.63. $C_{14}H_{18}O_2$. Calculated %: C 77.06, H 8.25.

The liquid portion of the substance was redistilled (b.p. 156-160° at 3 mm) and analyzed:

6.675 mg substance: 19.002 mg CO_2; 5.150 mg H_2O. 7.285 mg substance: 20.705 mg CO_2; 5.523 mg H_2O.
0.1696 g substance; 15.33 g benzene: Δt 0.25°. 0.0796 g substance; 15.94 g benzene: Δt 0.116°.
Found %: C 77.68, 77.58; H 8.63, 8.48. M 225.6, 219.5. $C_{14}H_{18}O_2$. Calculated %: C 77.06; H 8.25; M 218.

Condensation of the vinylacetylenic phenol (IV) with chloroacetic acid. 1 g of the substituted phenol (IV) was dissolved in 10 ml of a 10% solution of sodium hydroxide, 1.5 g of chloroacetic acid was added, and the mixture was heated on a boiling water bath for 1.5 hours. Then the liquid was acidified and extracted with ether, the ether extract being washed with a weak soda solution, and the resultant alkaline extract acidulated with dilute sulfuric acid. The precipitated acid (VIII) was filtered out; its m.p. was 80-81.5° after recrystallization from aqueous alcohol.

6.480 mg substance: 17.769 mg CO_2; 4.173 mg H_2O. 6.309 mg substance: 17.226 mg CO_2; 4.000 mg H_2O.
0.0436 g substance; 17 ml 0.01 N NaOH: 0.0186 g substance; 7.5 ml 0.01 N NaOH.
Found %: C 74.83, 74.52; H 7.25, 7.09. M 256.4, 248. $C_{16}H_{18}O_3$ Calculated %: C 74.42; H 6.98. M 258.

Condensation of 2,5-dimethyl-1,5-hexadien-3-yne with phenol. 19 g of 2,5-dimethyl-1,5-hexadien-3-yne was added drop by drop, with constant stirring, at 50° to a mixture of 18 g of phenol and 11 ml of phosphoric acid (sp. gr. 1.71). The liquid was heated to 45-50° for 15 hours and then processed as in the preceding experiment. The acid reaction products yielded 6.5 g of unreacted phenol (b.p. 60-65° at 4 mm) and 7.5 g of the substituted vinylacetylenic phenol (IV) with a b.p. of 126-129° at 2 mm (the polymer residue totaling 12 g). The product of the reaction of this phenol with chloroacetic acid had a melting point of 80-81°, and its mixed melting point with the preceding sample exhibited no depression.

The ether solution of the neutral products yielded 1 g of the initial substance (b.p. 45-49° at 4 mm) and 1 g of a substance with a b.p. of 105-146° at 5 mm; n_D^{20} 1.5407. The polymer residue totaled 1 g.

A crystalline, phosphorus-containing substance could be recovered from the condensation products of phenol with both the tetramethylbutynediol (I) and the dienyne (II) by the following procedure: The ether solution of the condensate was extracted with alkali, and the alkaline solution was acidulated with a dilute solution of hydrochloric acid, the resulting oily substance being separated from the water and a small amount of ether added to it. White crystals settled out, which had a m.p. of 137-139° (with decomposition) after recrystallization from aqueous alcohol. When the substance was calcined, a mineral residue was left behind; reacting an aqueous solution of this residue with uranyl yielded a white precipitate, evidence of the presence of sodium.

3.904 mg substance: 5.770 mg CO_2; 2.050 mg H_2O. 4.697 mg substance: 6.970 mg CO_2; 2.458 mg H_2O. 0.1068 g substance: 0.0298 g $Mg_2P_2O_7$ (Marie method). 0.1023 g substance: 0.0279 g $Mg_2P_2O_7$. Found %: C 40.33, 40.50; N 5.87, 5.86; P 7.77, 7.43. $C_{14}H_{16}ONa_2PO_4 \cdot 3H_2O$. Calculated %: C 40.18; H 5.26; P 7.4.

When 0.2763 g of the substance was dried to constant weight in a vacuum desiccator, it lost 0.0273 g, equivalent to 10.5% of crystallization water. The formula given above contains 12.9% of water.

The substance colors concentrated sulfuric acid crimson, dilution with water then producing a white precipitate. An aqueous solution of the substance yields a white precipitate with bromine water. It decolorizes a permanganate solution instantaneously.

Methylating the vinylacetylenic phenol (IV) with dimethyl sulfate. 10 grams of the substituted phenol were dissolved in 50 ml of 10% sodium hydroxide, and 12 ml of dimethyl sulfate was added gradually. The mixture was agitated for half an hour; the reaction was accompanied by the evolution of heat. Then sodium hydroxide solution was added until the reaction was alkaline, and the liquid was heated to boiling. After the solution had cooled, the product was extracted with ether, dried with potash, and distilled in vacuo after the ether had been driven off. This yielded 6.5 g of the methyl ester of the substituted phenol (VII) as a colorless, transparent liquid with a b.p. of 123-124° at 4.5 mm.

n_D^{20} 1.5340; d_4^{20} 0.9611; MR_D found 68.9; calculated 67.04.

3.485 mg substance: 10.771 mg CO_2; 2.716 mg H_2O. 3.080 mg substance: 9.503 mg CO_2; 2.405 mg H_2O. 0.1564 g substance; 16.05 g benzene: Δt 0.237°. 0.1242 g substance; 13.63 g benzene: Δt 0.216°. Found %: C 84.34, 84.20; H 8.72, 8.74. M 216.2, 215.3. $C_{15}H_{18}O$. Calculated %: C 84.12; H 8.41. M 214.

Hydrogenation of the vinylacetylenic phenol (IV). 1455 ml of hydrogen was absorbed in 8 hours (the theory calling for 1450 ml) when 405 g of the substance was hydrogenated in 50 ml of ethyl alcohol using an Adams platinum catalyst. The catalyst was then filtered out, the alcohol driven off, and the product distilled in vacuo. This yielded 3.2 g of the hydrogenated product (VI) as a colorless liquid with a b.p. of 131-132° at 4 mm.

n_D^{20} 1.5121; d_4^{20} 0.9551; MR_D found 64.77; calculated 64.69.

5.810 mg substance: 17.327 mg CO_2; 5.538 mg H_2O. 3.070 mg substance: 9.408 mg CO_2; 3.070 mg H_2O. Found %: C 81.4, 81.3; H 10.71, 10.87. $C_{14}H_{22}O$ Calculated %: C 81.55; H 10.73.

Methylation of the furanic phenol (XI). 16 grams of the furanic phenol (XI) (b.p. 156-160° at 3 mm) was dissolved in 100 ml of 10% sodium hydroxide, and 20 ml of dimethyl sulfate was gradually added. The mixture was agitated for half an hour, after which a solution of sodium hydroxide was added until its reaction was alkaline, and the liquid was heated to boiling. When the liquid had cooled, it was extracted with ether, dried with potash, and distilled in vacuo after the ether had been driven off. This yielded 9 g of the methyl ester of the furanic phenol (XII) with a b.p. of 127-127.5 at 2.5 mm.

n_D^{20} 1.5291; d_4^{20} 0.9988; MR_D found 71.8; calculated 68.27.

5.150 mg substance: 14.844 mg CO_2; 4.105 mg H_2O. 6.630 mg substance: 19.087 mg CO_2; 5.185 mg H_2O. 0.2392 g substance; 15.33 g benzene: Δt 0.343°. 0.1405 g substance; 15.33 g benzene: Δt 0.206°. Found %: C 78.64, 78.58; H 8.92, 8.75. M 232, 223.7. $C_{15}H_{20}O_2$. Calculated %: C 77.56; H 8.61; M 232.

Oxidation of the substituted anisole (VII) with permanganate. 38.1 grams of powdered permanganate was gradually added, with stirring and chilling with ice water, to a solution of 10 g of the substituted anisole (VII) in 150 g of acetone (the acetone had first been boiled with potassium permanganate for 8 hours and then distilled). Oxidation took 4 hours. The manganese dioxide was filtered out and thoroughly washed several times with hot water. The filtrates were combined and evaporated to small volume. A few drops of the filtrate threw down a white precipitate of calomel when reacted with mercuric chloride (test for formic acid). After the evaporated filtrate had cooled, it was acidulated with a 1% solution of sulfuric acid, yielding an oily substance that soon crystallized. The crystals were filtered out, washed a few times with cold water, and dried in a desiccator. This yielded 3.6 g of p-methoxyphenyldimethylacetic acid (IX), which had an m.p. of 87-88° after recrystallization from aqueous alcohol.

0.216 g substance: 11.5 ml 0.1 N NaOH. 0.109 g substance: 5.8 ml 0.1 N NaOH. Found M 188.2, 187.9. Calculated: M 194.

The mixed melting point of this substance with a known sample of *p*-methoxyphenyldimethylacetic acid exhibited no depression.

After the *p*-methoxyphenyldimethylacetic acid had been filtered out, the filtrate was neutralized with soda, evaporated on a water bath to small volume, acidulated with dilute sulfuric acid, and extracted with ether. The ether solution was dried with sodium sulfate and fractionated, yielding 1.5 g of a mixture of formic and acetic acids that boiled at 101-117°. When the acid mixture was reacted with mercuric chloride, it yielded a white precipitate of calomel, while heating it with a solution of silver nitrate threw down a black precipitate of metallic silver. These acids were mixed with strong sulfuric acid and heated to eliminate the formic acid. The addition of ethyl alcohol produced the characteristic odor of ethyl acetate, thus demonstrating that acetic acid was present.

Oxidation of the methyl ester of the furanic phenol (XII). a) 4.5 grams of pulverized permanganate was gradually added, with stirring and chilling with ice water, to a solution of 3.7 g of the substance in 80 ml of acetone. Oxidation lasted 7 hours. The manganese dioxide was filtered out and washed repeatedly with hot water. The filtrates were combined, evaporated to small volume (a few drops of the filtrate producing a white precipitate with mercuric chloride), and acidified with 1% sulfuric acid. This precipitated 0.95 g of crystals of anisic acid, which were filtered out and had an m.p. of 180-181° after recrystallization from water.

Found %: C 63.15, 63.19; H 5.39, 5.45. M 156.9, 152.8 $C_8H_8O_3$. Calculated %: C 63.13; H 5.3. M 152.

After the anisic acid crystals had been filtered out, the filtrate was neutralized with soda, evaporated to small volume, acidified with 1% sulfuric acid, and extracted with ether. Distillation of the ether solution yielded 0.5 g of formic acid with a b.p. of 101-104°, which produced a white calomel precipitate when reacted with a solution of mercuric chloride.

b) 2.9 grams of the substance was placed in a solution of 0.5 g of potash in 100 ml of water. The resulting mixture was vigorously stirred for 3 hours, and then 9.6 g of finely pulverized potassium permanganate was added. The manganese dioxide was filtered out and washed repeatedly with water. 60 ml of water and the volatile neutral products were distilled from the combined filtrates (180 ml), which exhibited a positive iodoform reaction. The distillate was chilled with ice and saturated with potash, and 20 ml was again driven off, the next distillate being again saturated with potash, and 5 ml of liquid being driven off – the last distillate exhibiting the distinct odor of acetone. The 2,4-dinitrophenylhydrazone of this distillate was prepared, its mp. being 125-126° after recrystallization from ethyl alcohol. Its mixed melting point with the known 2,4-diphenylhydrazone of acetone exhibited no depression.

After the neutral products had been driven off, the filtrate was acidified with 1% sulfuric acid, throwing down white crystals whose m.p. was 180-181° after recrystallization from water. Their mixed melting point with anisic acid exhibited no depression. After the crystals of anisic acid had been filtered out, the filtrate was distilled, the distillate yielding a white calomel precipitate (formic acid) with mercuric chloride.

SUMMARY

Condensing tetramethylbutynediol with phenol in the presence of phosphoric acid yields a parasubstituted vinylacetylenic phenol (IV) and a phenolic derivative of dihydrofuran (XI).

When 2,5-dimethyl-1,5-hexadien-3-yne was condensed with phenol under the same conditions all we got was the parasubstituted vinylacetylenic phenol (IV), no furanic phenol (XI) being produced.

Methylation of the vinylacetylenic phenol (IV) with dimethyl sulfate yields the methyl ester (VII); catalytic hydrogenation with a Pt catalyst yields the saturated substituted phenol (VI); and condensation with chloroacetic acid yields the derivative (VIII). Oxidation of the vinylacetylenic phenol (IV) with permanganate yields formic, acetic, and *p*-methoxyphenyldimethylacetic acids.

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[2] Yu. Zalkind, V. Teterin, and S. Kuznetsov, *J. Gen. Chem.* 15, 488 (1945).

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Received July 2, 1950

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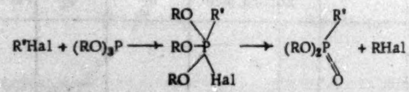
THE ADDITION OF DIALKYLPHOSPHOROUS ACIDS TO UNSATURATED COMPOUNDS

III. A NEW METHOD OF SYNTHESIZING β-KETOPHOSPHINIC ESTERS

A. N. Pudovik

Of the present methods of synthesizing phosphinic acid esters and their derivatives known in the literature, the most important and most widely used is the method developed by Academician A. E. Arbuzov, and put forward by him in 1905 [1]. As we know, this method involves the action of esters of phosphorous acid upon organic compounds containing halogen; it may be represented, in general, as follows:



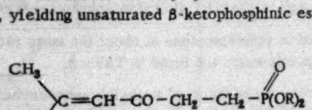
This reaction has been utilized by A. E. Arbuzov and B. A. Arbuzov and their pupils [2], as well as by other authors, to synthesize a large number of phosphinic esters of differing structure, containing various aliphatic and aromatic radicals.

The method based upon the reaction of halogen-containing organic compounds with salts of dialkylphosphorous acids is of much less importance in the synthesis of esters of phosphinic acids. This reaction, which was first investigated by Michaelis and Becker [3], was subsequently elaborated and employed with considerable success by Nylen [4], A. E. Arbuzov and B. A. Arbuzov [5], G. Kh. Kama, and others.

Other methods of synthesizing esters of the phosphinic acids [6] known at the present time have not been widely employed in laboratory practice and are of purely theoretical interest.

In our 1947-1948 study of the reactions of halogen allyl isomers and salts of dialkylphosphinic acids, we found [7] that the reaction involves the addition of sodium diethylphosphite at the double bond of the unsaturated phosphinic esters, forming alkoxydi-(dialkylphospho)-pentanes. This interesting observation then served in the elaboration of a new method for preparing esters of phosphinic acids, involving the addition of dialkylphosphorous acids to α,β-unsaturated electronophilic reagents in the presence of alcoholates of the alkali metals.

In our previous research on this topic [8] we showed that dialkylphosphorous acids are added with extraordinary ease to acrylonitrile, methyl methacrylate, and β,β-dimethyl divinyl ketone. When equimolecular proportions of the dialkylphosphorous acids and the ketone are employed in the last of these three cases, addition occurs only at the unsubstituted vinyl group, yielding unsaturated β-ketophosphinic esters of the following general type:



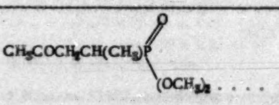
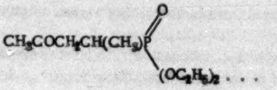
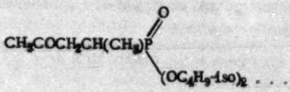
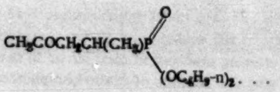
The ability to add a carbonyl group and a substituted vinyl group is greatly reduced in β,β-dimethyl divinyl ketone, the addition of the alkylphosphorous acid taking place only after addition at the unsubstituted vinyl group is complete.

Continuing this research, we felt it would be highly interesting and important to make a more thorough and extensive study of the addition of dialkylphosphorous acids to the simplest α,β-ketones containing a vinyl group substituted at various positions, with different radicals and with varying degree of addition, and to learn the effect of the nature, quantity, and position of these radicals upon the activity of the double bond and of the carbonyl group in addition reactions. We chose ethylidene acetone, benzalacetone, and furfuralacetone for this investigation, as derivatives of methyl vinyl ketone that contain substituents at the β-carbon atom of the vinyl group.

The procedure employed was the usual one: a saturated alcoholic solution of a sodium alcholate was added drop by drop to a mixture of the dialkylphosphorous acid and the unsaturated ketone. Considerable heat was evolved during the reaction, and the viscosity of the reaction mixture rose substantially. After enough of the alcoholate had been added (the reaction mixture no longer warmed up), the reaction mass was distilled in vacuo. Analysis of the resultant addition products by the Tserevitinov method indicated that they did not contain any hydroxyl group and, hence, were ketophosphinic esters rather than hydroxyphosphinic esters (which could have been formed if the dialkylphosphorous acids had been added at the carbonyl group of the unsaturated ketones).

The dialkylphosphorous acids were added most readily and rapidly to ethylidene acetone. Yields of 62-75% of the addition products, the respective 1-methyl-1-dialkylphosphobutanones-3, were obtained. The constants of the synthesized ketophosphinic esters are listed in Table 1.

TABLE 1

No.	Formula	Boiling point	n_D^{20}	d_4^{20}	Per cent yield
1	 $CH_3COCH_2CH(CH_3)P\genfrac{}{}{0pt}{}{\diagup O}{\diagdown (OCH_3)_2}$	134 - 135° (10 mm)	1.4411	1.1313	69.1
2	 $CH_3COCH_2CH(CH_3)P\genfrac{}{}{0pt}{}{\diagup O}{\diagdown (OC_2H_5)_2}$ . . .	139 - 140 (10 mm)	1.4387	1.0850	62.1
3	 $CH_3COCH_2CH(CH_3)P\genfrac{}{}{0pt}{}{\diagup O}{\diagdown (OC_4H_9\text{-iso})_2}$ . . .	156 - 158 (10 mm)	1.4400	1.0221	63.7
4	 $CH_3COCH_2CH(CH_3)P\genfrac{}{}{0pt}{}{\diagup O}{\diagdown (OC_4H_9\text{-n})_2}$ . . .	172 - 173 (10 mm)	1.4412	0.9985	74.4

Dialkylphosphorous acids are added to benzalacetone more slowly than to ethylidene acetone, though the reaction is just as vigorous, with considerable heat liberated by the reaction mixture. The constants and yields of the synthesized β-ketophosphinic esters, 1-phenyl-1-dialkylphosphobutanones-3, are listed in Table 2.

The dialkylphosphorous acids are added to furfuralacetone at about the same rate as to benzalacetone. The constants of the synthesized β-ketophosphinic esters are listed in Table 3.

In all the investigated reactions involving the addition of dialkylphosphorous acids to unsaturated ketones the addition velocity falls substantially as the molecular weight of the radicals entering into the composition of the dialkylphosphorous acids increases. Hence, the only way to secure more complete and more rapid reactions, especially when dibutyl- and diisobutylphosphorous acids are added, is either to heat the reaction mixture after a given quantity of the saturated alcoholic solution of the alcoholate has been added or to add an excess of the alcholate to the reaction mixture until the exothermal effect ceases. It is likewise of great importance to the producing of pure β-ketophosphinic ethers that the alcoholic solution of a sodium alcoholate employed as a catalyst be prepared from an alcohol containing the same radical as the one entering into the composition of the dialkylphosphorous acid added. The reason for this is that a partial exchange of radicals occurs during the reaction, as we have discovered, between the molecules of the alcohol and the dialkylphosphorous acid:

$$2CH_3OH + (C_4H_9O)_2POH \xrightarrow{CH_3ONa} 2C_4H_9OH + (CH_3O)_2POH,$$

TABLE 2

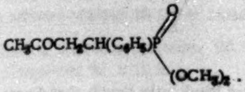
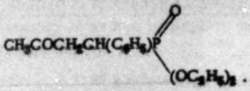
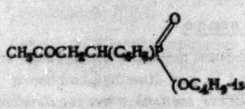
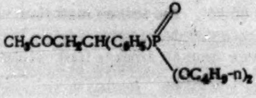
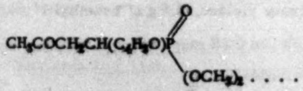
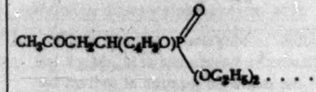
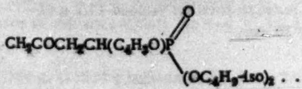
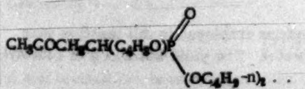
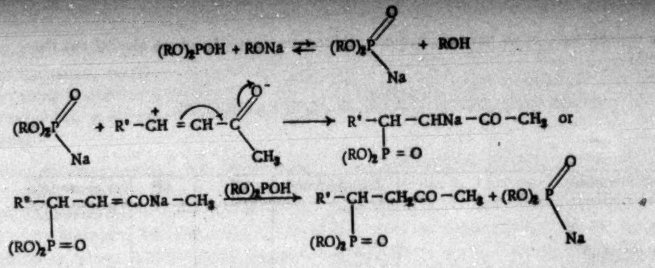
No.	Formula	Boiling point	n_D^{20}	d_4^{20}	Per cent yield
1	 $CH_3COCH_2CH(C_6H_5)P(=O)(OCH_3)_2$	189 - 190° (10 mm)	1.5095	1.1791	64.6
2	 $CH_3COCH_2CH(C_6H_5)P(=O)(OC_2H_5)_2$	203 (16 mm)	1.5050	1.1309	55.8
3	 $CH_3COCH_2CH(C_6H_5)P(=O)(OC_4H_9\text{-iso})_2$	208 (12 mm)	1.4900	1.0736	64.5
4	 $CH_3COCH_2CH(C_6H_5)P(=O)(OC_4H_9\text{-n})_2$	219 - 220 (13 mm)	1.4927	1.0737	63.0

TABLE 3

No.	Formula	Boiling point	n_D^{20}	d_4^{20}	Per cent yield
1	 $CH_3COCH_2CH(C_4H_9O)P(=O)(OCH_3)_2$	163 - 164° (6 mm)	1.4835	1.2181	44.7
2	 $CH_3COCH_2CH(C_4H_9O)P(=O)(OC_2H_5)_2$	192 - 193 (16 mm)	1.4755	1.1616	62.0
3	 $CH_3COCH_2CH(C_4H_9O)P(=O)(OC_4H_9\text{-iso})_2$	161 (3 mm)	1.4711	1.0932	72.1
4	 $CH_3COCH_2CH(C_4H_9O)P(=O)(OC_4H_9\text{-n})_2$	182 (4 mm)	1.4730	1.0995	60.0

resulting in the formation of a dialkylphosphorous acid with a different radical and in contaminating the principal reaction product due to the addition of this new acid to the unsaturated ketone.

The general pattern for the addition of dialkylphosporous acids to unsaturated ketones that contain one substituted group attached to the β-carbon atom of the vinyl group may be represented as follows:



The acids produced by saponifying the synthesized ketophosphinic esters are thick, oily liquids that do not crystallize upon standing.

EXPERIMENTAL

Addition of Dialkylphosphorous Acids to Ethylideneacetone

1. Addition of dimethylphosphorous acid. A saturated solution of sodium methylate in methanol was added slowly, drop by drop, to a mixture of 8.4 g of ethylidene acetone and 11 g of dimethylphosphorous acid. The reaction mixture heated up considerably; the addition of the sodium methylate was regulated so as to keep the temperature of the reaction mixture from going higher than 60-70°. The sodium methylate was added until no more heat was evolved by the reaction mixture. The viscosity of the reaction mixture rose appreciably during the course of the reaction. Fractionation of the mixture from an Arbuzov flask yielded 13.4 g of 1-methyl-1-dimethylphosphobutanone-3 with a b.p. of 134-135° at 10 mm.

0.1326 g, 0.1300 g substance: 32.1 ml, 31.0 ml NaOH (T = 0.024417).
Found %: P 15.8, 16.1. $C_7H_{15}O_4P$. Calculated %: P 15.9.

2. Addition of diethylphosphorous acid. A saturated solution of sodium ethylate in ethyl alcohol was added a drop at a time to a mixture of 8.4 g of ethylidene acetone and 14 g of diethylphosphorous acid. After the reaction was complete, fractionation of the reaction mixture yielded 13.9 g of 1-methyl-1-diethylphosphobutanone-3 with a b.p. of 139-140° at 10 mm.

0.1302 g, 0.0978 g substance: 26.5 ml 20.4 ml NaOH (T = 0.024417).
Found %: P 13.8, 14.1. $C_7H_{19}O_4P$. Calculated %: P 14.0.

3. Addition of diisobutylphosphorous acid. A solution of sodium isobutylate in isobutyl alcohol was added to a mixture of 8.4 g of ethylidene acetone and 18.6 g of diisobutylphosphorous acid. Much less heat was evolved than in the preceding reactions. The amount of the saturated solution of sodium isobutylate that was added totaled some 2 ml. Fractionation of the reaction mixture yielded 17.2 g of 1-methyl-1-diisobutylphosphobutanone-3 with a b.p. of 156-158° at 10 mm.

0.1186 g substance: 20.0 ml NaOH (T = 0.024417).
Found %: P 11.6. $C_{13}H_{27}O_4P$. Calculated %: P 11.2.

4. Addition of dibutylphosphorous acid. The amounts of reagents employed in this reaction were the same as in the preceding one, sodium butylate being used, however. The yield was 20.1 g of 1-methyl-1-dibutylphosphobutanone-3 with a b.p. of 172-173° at 10 mm.

0.1248 g substance: 20.7 ml NaOH (T = 0.024417).
Found %: P 11.20 $C_{13}H_{27}O_4P$. Calculated %: P 11.20.

Addition of Dialkylphosphorous Acids to Benzalacetone

The experimental procedure employed resembled that described in the preceding experiments.

1. Addition of dimethylphosphorous acid. 10 g of benzalacetone and 7.5 g of dimethylphosphorous acid in the presence of sodium methylate yielded 11.3 g of 1-phenyl-1-dimethylphosphobutanone-3 with a b.p. of 189-190° at 10 mm.

0.1792 g substance: 39.8 ml NaOH (T = 0.019404). Found %: P 11.9. $C_{12}H_{17}O_4P$. Calc.%: P 12.1.

2. Addition of diethylphosphorous acid. A saturated solution of sodium ethylate in ethyl alcohol was added to a mixture consisting of 12 g of benzalacetone and 12 g of diethylphosphorous acid. Fractionation of the reaction mixture yielded 13.4 g of 1-phenyl-1-diethylphosphobutanone-3 with a b.p. of 203° at 16 mm.

0.1336 g, 0.1316 g substance: 26.7 ml, 26.7 ml NaOH (T = 0.019404). Found %: P 10.8, 10.9. $C_{14}H_{21}O_4P$. Calculated %: P 10.9.

3. Addition of diisobutylphosphorous acid. 7.3 g of benzalacetone and 10 g of diisobutylphosphorous acid in the presence of sodium isobutylate yielded 11.2 g of 1-phenyl-1-diisobutylphosphobutanone-3 with a b.p. of 208° at 12 mm.

0.1426 g, 0.1188 g substance: 25.2 ml, 20.5 ml NaOH (T = 0.019404). Found %: P 9.4, 9.2. $C_{18}H_{29}O_4P$. Calculated %: P 9.1.

4. Addition of dibutylphosphorous acid. 10.8 g of benzalacetone and 15 g of dibutylphosphorous acid yielded 16.2 g of 1-phenyl-1-dibutylphosphobutanone-3 with a b.p. of 219-220° at 13 mm.

0.1340 g substance: 24.4 ml NaOH (T = 0.019404). Found %: P 9.6. $C_{18}H_{29}O_4P$. Calculated %: P 9.1.

Addition of Dialkylphosphorous Acids to Furfuralacetone

1. Addition of dimethylphosphorous acid. 10 g of furfuralacetone and 9 g of dimethylphosphorous acid in the presence of sodium methylate yielded 8.5 g of 1-furyl-1-dimethylphosphobutanone-3 with a b.p. of 163-164° at 6 mm.

0.1178 g substance: 28.1 ml NaOH (T = 0.019404). Found %: P 12.8. $C_{10}H_{15}O_5P$. Calculated %: P 12.6.

2. Addition of diethylphosphorous acid. 10 g of furfuralacetone and 10 g of diethylphosphorous acid in the presence of sodium ethylate yielded 12.4 g of 1-furyl-1-diethylphosphobutanone-3 with a b.p. of 192-193° at 16 mm.

0.1630 g, 0.1270 g substance: 34.5 ml, 27.0 ml NaOH (T = 0.019404). Found %: P 11.4, 11.3. $C_{12}H_{19}O_5P$. Calculated %: P 11.3.

3. Addition of diisobutylphosphorous acid. 13.7 g of furfuralacetone and 21.0 g of diisobutylphosphorous acid yielded 25 g of 1-furyl-diisobutylphosphobutanone-3 with a b.p. of 161° at 3 mm.

0.1110 g substance: 19.6 ml NaOH (T = 0.019404). Found %: P 9.5. $C_{16}H_{27}O_5P$. Calc.%: P 9.4.

4. Addition of dibutylphosphorous acid. 7 g of furfuralacetone and 11 g of dibutylphosphorous acid in the presence of sodium butylate yielded 10.8 g 1-furyl-1-dibutylphosphobutanone-3 with a b.p. of 182° at 4 mm.

0.1104 g, 0.1214 g substance: 20.0 ml, 21.8 ml NaOH (T = 0.019404). Found %: P 9.7, 9.3. $C_{16}H_{27}O_5P$. Calculated %: P 9.4.

SUMMARY

1. A new method has been developed for synthesizing β-ketophosphinic esters by adding dialkylphosphorous acids to α, β-unsaturated ketones in the presence of alcoholates of alkali metals.

2. The addition products of dimethyl-, diethyl-, diisobutyl-, and dibutyl-phosphorous acids to ethylidene acetone, benzalacetone, and furfuralacetone have been isolated and identified.

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Received June 2, 1950

THE ADDITION OF DIALKYLPHOSPHOROUS ACIDS TO UNSATURATED COMPOUNDS

IV. THE ADDITION OF DIALKYLPHOSPHOROUS ACIDS TO UNSATURATED ALDEHYDES

A NEW METHOD OF SYNTHESIZING UNSATURATED α-HYDROXYPHOSPHINIC ESTERS

A. N. Pudovik and Yu. P. Kitaev

In our previous report [1] we described the addition of dialkylphosphorous acids to some electronophilic reagents belonging to the group of unsaturated nitriles, acid esters, and ketones. We showed that when catalysts—alcoholates of the alkali metals—are present, addition takes place very readily at the double bond, resulting in the formation of derivatives of phosphinic esters. This discovery of a new method of synthesizing phosphinic esters made cyanophosphinic, carboxylalkylphosphinic, and ketophosphinic esters of diversified structure highly accessible, though their preparation by the other methods known at the present time sometimes involved substantial preparative difficulties.

In the present research we decided to employ our newly discovered reaction of the addition of dialkylphosphorous acids to unsaturated electronophilic reagents to α,β-unsaturated aldehydes, using it to synthesize hitherto unknown esters of aldehydophosphinic acids. The substances we proposed to employ were acrolein, crotonaldehyde, furylacroline, cinnamaldehyde, and hexadienal.

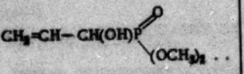
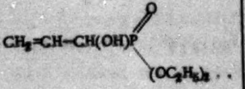
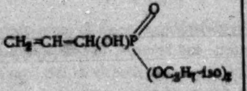
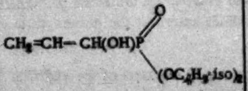
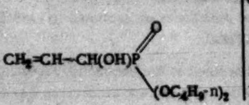
We introduced some changes into the reaction procedure described in our preceding papers to increase the yield of the addition products. A saturated alcoholic solution of a sodium alcoholate was added dropwise to a mixture of equimolecular quantities of the unsaturated aldehyde and the dialkylphosphorous acid. Considerable heat was evolved during the reaction, the addition of the alcoholate being stopped as soon as the evolution of heat by the reaction mixture ceased. To avoid losses, the addition reaction was performed directly in an Arbuzov flask in the presence of a small amount of hydroquinone, which protected the unsaturated aldehyde against polymerization during the course of the reaction and during fractionation. With the same objective in view, the sodium alcoholate present in the reaction mixture was neutralized by the addition of a few drops of glacial acetic acid before fractionation was begun. When the end products were solids that were soluble with difficulty in organic solvents, the reactions were carried out in an alcohol solution; the addition products settled out of the solution as crystalline precipitates and were then recrystallized from a water-alcohol mixture.

Of all the unsaturated aldehydes used, dialkylphosphorous acids are added most readily and rapidly to acrolein. Much less catalyst was required to complete the reaction when dimethyl- and diethylphosphorous acids were added than in the addition of the higher dialkylphosphorous acids. As we have stated in our preceding paper [2], the purest products are obtained when the alcoholates, the alcohols, and the dialkylphosphorous acids all contained the same radicals.

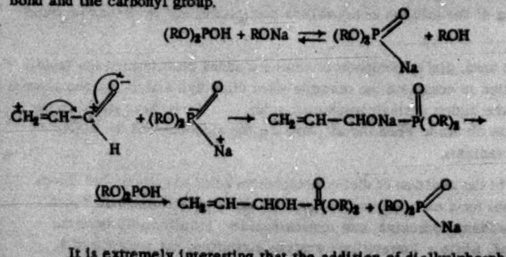
A study of some of the products of the addition of dialkylphosphorous acids to acrolein has shown that they display no characteristic reactions for a carbonyl group, more specifically failing to react with hydroxylamine, phenylhydrazine, p-dinitrophenylhydrazine, and semicarbazide. Titration with bromine indicated that they possessed a double bond, while a Tserevitinov analysis established the presence of a hydroxyl group. Our findings led us to conclude that the addition products were not aldehydo-phosphinic esters, as we had presupposed, but unsaturated hydroxyphosphinic esters, so that dialkylphosphorous acids are not added to unsaturated aldehydes at the double bond, but at the carbonyl group.

The constants and yields of the synthesized unsaturated α-hydroxyphosphinic esters are listed in Table 1.

TABLE 1

Compound No.	Formula	B.p.	n_D^{20}	d_4^{20}	MR_D Found	MR_D Calculated	% Yield
1	 $CH_2=CH-CH(OH)P(=O)(OCH_3)_2$	149-151° (13 mm)	1.4572	1.2188	37.1	37.2	66.2
2	 $CH_2=CH-CH(OH)P(=O)(OC_2H_5)_2$	154-155 (13 mm)	1.4506	1.1225	46.5	46.5	77.1
3	 $CH_2=CH-CH(OH)P(=O)(OC_3H_7\text{-iso})_2$	140-141 (7 mm)	1.4415	1.0465	56.1	55.7	69.8
4	 $CH_2=CH-CH(OH)P(=O)(OC_4H_9\text{-iso})_2$	168-170 (13 mm)	1.4348	0.9968	65.4	64.9	14.0
5	 $CH_2=CH-CH(OH)P(=O)(OC_4H_9\text{-n})_2$	169-172 (13 mm)	1.4411	1.0130	65.2	64.9	15.0

The esters are colorless, mobile liquids with a peculiar fish-oil odor. They are freely soluble in organic solvents. Their formation may be represented as follows: (See below). In their addition to acrolein, therefore, the dialkylphosphorous acids behave very much like many other reagents, such as hydrogen cyanide and sodium bisulfite, which are also added at the carbonyl group for the most part. The contrast in the behavior of structurally similar aldehydes and ketones in addition reactions may be attributed to the fact that in the latter the electronophilic nature of the carbon atom in the carbonyl group is greatly reduced, owing to the steric and electronic (+I effect) influence of the substituent R group, so that the double bond proves to be more active during addition. From this standpoint considerable interest is attached to a study of the addition reactions of dialkylphosphorous acids to unsaturated ketones possessing two substituents attached to the β-carbon atom of the vinyl group, say, to mesityl oxide and others, in which the electronophilic nature of the end carbon atom ought to be greatly reduced and, hence, addition ought to take place at both the double bond and the carbonyl group.



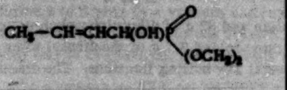
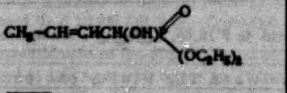
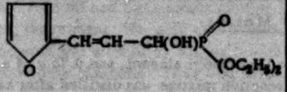
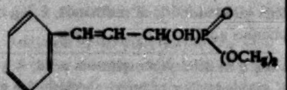
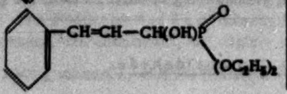
$$(RO)_2POH + RONa \rightleftarrows (RO)_2P(=O)Na + ROH$$

$$\overset{+}{C}H_2=CH-C(=O^-)H + (RO)_2\overset{-}{P}(=O)\overset{+}{Na} \longrightarrow CH_2=CH-CHONa-P(=O)(OR)_2 \longrightarrow$$

$$\xrightarrow{(RO)_2POH} CH_2=CH-CHOH-P(=O)(OR)_2 + (RO)_2P(=O)Na$$

It is extremely interesting that the addition of dialkylphosphorous acids to crotonaldehyde is much less smooth than to acrolein. The yields of the addition products of dimethyl- and diethylphosphorous acids to crotonaldehyde turned out to be very low, while no addition products could be recovered at all in the case of the dibutyl- and diisobutylphosphorous acids. The addition of dimethylphosphorous acid to furylacrolein and cinnamaldehyde produces yields that are nearly quantitative, the addition products being crystalline substances that were freely soluble in organic solvents but only slightly soluble in cold water. Tserevitinov analysis of these products indicated that they contained a hydroxyl group and, hence, also unsaturated hydroxyphosphinic esters. The constants of the addition products of the dialkylphosphorous acids to crotonaldehyde, furylacrolein, and cinnamaldehyde are given in Table 2.

TABLE 2

Compound No.	Formula	B.p.	M.p.	n_D^{20}	d_4^{20}	% Yield
1		150-152° (8 mm)	–	1.4630	1.1690	–
2		163-164 (9 mm)	–	1.4555	1.1005	–
3		–	106-107°	–	–	87.2
4		–	101-102	–	–	87.0
5		–	104-105	–	–	75.4

Finally, we investigated the addition of dimethylphosphorous and diethylphosphorous acids to hexadien-2,4-al-1. The reaction is fairly vigorous, considerable heat being evolved. Processing and fractionation of the reaction mixtures produced small yields of the following addition products: 1-dimethylphosphohexadien-4-2,4-ol-1, with a b.p. of 153-154° (13 mm); n_D^{20} 1.4866, d_4^{20} 1.1165, and 1-diethylphosphohexadien-2,4-ol-1, with a b.p. of 167-168° (17 mm); n_D^{20} 1.4774, d_4^{20} 1.0717.

The diene hydroxyphosphinic esters are faintly yellow liquids with a peculiar odor, which are readily soluble in alcohol and in ether.

EXPERIMENTAL

I. Addition of Dialkylphosphorous Acids to Acrolein,

1. Addition of dimethylphosphorous acid. A small quantity (about 15 drops) of a saturated solution of sodium methylate was added drop by drop to a reaction mixture consisting of 7.5 g of acrolein stabilized with hydroquinone and 15 g of dimethylphosphorous acid in a small Arbuzov flask, the flask being cooled with water. The reaction was violent, the reaction mixture becoming very hot. After the sodium methylate had been neutralized by adding acetic acid, the reaction mixture was fractionated in vacuo, yielding 12 g of the methyl ester of 1-hydroxy-2-propene-1-phosphinic acid (Table 1, Compound 1).

0.1394 g substance: 52.5 ml NaOH (T = 0.01768). Found %: P 18.45. $C_5H_{11}O_4P$. Calc.%: P 18.68.

The 1-hydroxy-2-propene-1-phosphinic acid, secured by saponifying the ester with dilute hydrochloric acid, was a thick, oily, light-brown liquid that did not crystallize upon standing.

2. Addition of diethylphosphorous acid. About 40 drops of a saturated alcoholic solution of sodium ethylate was added to a mixture consisting of 7 g of acrolein and 22.3 g of diethylphosphorous acid. Fractionation of the reaction mixture yielded 19 g of the ethyl ester of 1-hydroxy-2-propene-1-phosphinic acid. (Table 1, Compound 2).

0.1060 g substance: 43.40 ml NaOH (T = 0.01768). Found %: P 16.34. $C_7H_{15}O_4P$. Calc.%: P 15.98.

3. Addition of diisopropylphosphorous acid. 2.5 g of acrolein and 5.4 g of diisopropylphosphorous acid, under conditions similar to those described for the preceding experiments, yielded 5.3 g of the diisopropyl ester of 1-hydroxy-2-propene-1-phosphinic acid (Table 1, Compound 3).

0.1002 g substance: 27.9 ml NaOH (T = 0.01768). 0.1103 g substance: 13.05 ml CH_4.
Found %: P 13.66; OH 7.91. $C_9H_{19}O_4P$. Calculated %: P 13.96; OH 7.65.

4. Addition of diisobutylphosphorous acid. 5.3 g of acrolein and 15.7 g of diisobutylphosphorous acid yielded 4.5 g of the diisobutyl ester of 1-hydroxy-2-propene-1-phosphinic acid (Table 1, Compound 4), plus several low-boiling fractions.

0.2132 g substance: 54.5 ml NaOH (T = 0.01768). Found %: P 12.52. $C_{11}H_{23}O_4P$. Calculated %: P 12.40.

5. Addition of dibutylphosphorous acid. 10.2 g of acrolein and 32 g of dibutylphosphorous acid were used for the reaction. Repeated fractionation of the reaction mixture yielded 3.7 g of the dibutyl ester of 1-hydroxy-2-propene-1-phosphinic acid (Table 1, Compound 5), plus several low-boiling fractions. The fractionation residue totaled 20 g.

0.2093 g substance: 54.1 ml NaOH (T = 0.01768). Found %: P 12.65. $C_{11}H_{23}O_4P$. Calculated %: P 12.40.

II. Exchange of Radicals Between the Alcohols and The Dialkylphosphorous Acids in the Presence of Alcoholates of the Alkali Metals.

Experiment 1. 10.8 g of dimethylphosphorous acid, 14.1 g of butyl alcohol, and 0.75 g of a saturated solution of sodium methylate were placed in an Arbuzov flask. The reaction mixture was distilled after having been allowed to stand for twenty minutes at room temperature. This yielded 5.5 g of methanol, 5.9 g of butyl alcohol, 3.8 g of dimethylphosphorous acid, and 4.9 g of dibutylphosphorous acid.

Experiment 2. A similar reaction was carried out with 9.6 g of dibutylphosphorous acid, 4 g of methanol, and 0.35 g of a saturated solution of sodium methylate. This yielded 1.5 g of butyl alcohol, 0.5 g of dimethylphosphorous acid, and 6.1 g of dibutylphosphorous acid.

III. Addition of Dialkylphosphorous Acids to Crotonaldehyde.

1. Addition of dimethylphosphorous acid. Some 60 drops of an alcoholic solution of sodium methylate was gradually added from a dropping funnel to a chilled mixture of 5 g of crotonaldehyde and 11.6 g of dimethylphosphorous acid. Repeated fractionation of the reaction products yielded 0.85 g of the methyl ester of 1-hydroxy-2-butene-1-phosphinic acid (Table 2, Compound 1), plus several low-boiling fractions. The fractionation residue totaled 8.9 g.

0.1604 g substance: 57.18 ml NaOH (T = 0.01768). Found %: P 17.45. $C_6H_{13}O_4P$. Found %: P 17.23.

2. Addition of diethylphosphorous acid. 5.1 g of crotonaldehyde and 12.9 g of diethylphosphorous acid yielded 1.5 g of the diethyl ester of 1-hydroxy-2-butene-1-phosphinic acid (Table 2, Compound 2), plus several low-boiling fractions.

0.2061 g substance: 60.24 ml NaOH (T = 0.01768). Found %: P 14.64. $C_8H_{17}O_4P$. Calculated %: P 14.90.

Saponification of the ester by heating it with dilute hydrochloric acid yielded 1-hydroxy-2-butene-1-phosphinic acid as a thick, oily liquid that did not crystallize upon standing.

IV. Addition of Diethylphosphorous Acid to Furylacrolein.

6.5 g of furylacrolein (m.p. 52.5°) and 7.8 g of diethylphosphorous acid were dissolved in 24 ml of absolute ethyl alcohol. The color of the solution turned from yellow to cherry-red when 10 drops of a saturated alcoholic solution of sodium ethylate was added. Considerable heat was evolved by the reaction mixture. After some more sodium ethylate (20 drops) had been added and the reaction mixture had been heated on a water bath for an hour, a crystalline precipitate began to settle out. Chilling the flask caused 8.6 g of a crystalline precipitate as white leaflets to settle out. Evaporation of the mother liquor yielded another 3 g of the crystalline product. The m.p. of the product was 106-107° after it had been dried in a vacuum desiccator.

0.1681 g substance: 40.17 ml NaOH (T = 0.01768). Found %: P 11.99. $C_{11}H_{17}O_5P$. Calculated %: P 11.92.

We were unable to secure any crystalline addition products in similar reactions of furylacrolein with dimethylphosphorous and dibutylphosphorous acid. The addition products were thick oily liquids that did not crystallize upon standing and did not distil in vacuo.

V. Addition of Dialkylphosphorous Acids to Cinnamaldehyde.

1. Addition of dimethylphosphorous acid. A saturated solution of sodium methylate in methanol was added drop by drop to a reaction mixture consisting of 4.6 g of cinnamic aldehyde and 4 g of dimethylphosphorous acid. The mixture heated up considerably (to +75°) and grew much more viscous. The contents of the flask crystallized into a solid yellow mass after standing for one hour at room temperature. Recrystallization from an aqueous-alcoholic solution and drying in a vacuum desiccator yielded 7 g of the dimethyl ester of 1-hydroxy-3-phenyl-2-propene-1-phosphinic acid as minute colorless crystals. The crystals were freely soluble in alcohol, ether, benzene, and chloroform, less so in gasoline, and sparingly soluble in water.

0.2024 g substance: 53.2 ml NaOH (T = 0.01768). 0.0853 g substance: 8.9 ml CH_4.
Found %: P 12.86; OH 7.28. $C_{11}H_{15}O_4P$. Calculated %: P 12.81; OH 7.02.

Saponification of the dimethyl ester of 1-hydroxy-3-phenyl-2-propene-1-phosphinic acid. 2.4 g of the ester was heated to 100° in a sealed tube for 19 hours with 30 ml of dilute hydrochloric acid. After the methyl chloride had been driven off and the aqueous solution had been boiled with activated charcoal, the solution was evaporated to a thick, tacky mass. No acid crystallized out despite the long time the mass was allowed to stand. A barium salt of the acid was secured by boiling it with barium carbonate. The salt crystallized from the concentrated solution as tiny white platelets. They were dried at 110-120° and analyzed for their barium content.

0.1439 g substance: 0.0598 g $BaSO_4$. Found %: Ba 24.44. $C_{18}H_{20}O_8P_2Ba$. Calculated %: Ba 24.37.

2. Addition of diethylphosphorous acid. 4.07 g of diethylphosphorous acid and 4.05 g of cinnamic aldehyde were used for the reaction, which was carried out as in the addition of the dimethylphosphorous acid. The reaction yielded a crystalline product that had a m.p. of 104-105° after having been recrystallized from a water-alcohol solution. The product totaled 6 g of minute, faintly yellow needles with the odor of cinnamon, soluble in alcohol, ether, benzene, and chloroform, and slightly soluble in water.

0.1949 g substance: 42.1 ml NaOH (T = 0.01768). Found %: P 11.58. $C_{13}H_{19}O_4P$. Calculated %: P 11.48.

The addition of dibutylphosphorous and diisobutylphosphorous acids to cinnamaldehyde yielded thick, oily products that did not crystallize upon standing and could not be distilled in vacuo without decomposing.

VI. Addition of Dialkylphosphorous Acids to Hexadien-2,4-al-1.

1. Addition of dimethylphosphorous acid. 5.1 g of hexadien-2,4-al-1 and 6 g of dimethylphosphorous acid were placed in a small Arbuzov flask. As the sodium methylate was added drop by drop, the reaction mixture grew very hot. Double fractionation yielded about 2 g of the addition product — 1-dimethylphosphohexadien-2,4-ol-1 with a b.p. of 153-154° (13 mm); n_D^{20} 1.4866, d_4^{20} 1.1165.

0.1676 g substance: 50.3 ml NaOH (T = 0.01786). Found %: P 14.69. $C_8H_{15}O_4P$. Calculated %: P 15.02.

2. Addition of diethylphosphorous acid. The reaction of 7.5 g of diethylphosphorous acid with 5.2 g of the hexadienal yielded 1.4 g of 1-diethylphosphohexadien-2,4-ol-1 with a b.p. of 167-168° (17 mm); n_D^{20} 1.4774, d_4^{20} 1.0717.

0.1020 g substance: 28.5 ml NaOH (T = 0.01768). Found %: P 13.70. $C_{10}H_{19}O_4P$. Calculated %: P 13.22.

1-Diethylphosphohexadien-2,4-ol-1 is a thick, yellow liquid with a peculiar odor that is freely soluble in alcohol and ether.

SUMMARY

1. It has been shown that dialkylphosphorous acids are added to α,β-unsaturated aldehydes at the carbonyl group in the presence of alcoholates of the alkali metals, giving rise to esters of unsaturated α-hydroxyphosphinic acids.

2. The addition products of dialkylphosphorous acids to acrolein, cinnamaldehyde, crotonaldehyde, furylacrolein, and hexadien-2,4-al-1 have been prepared and identified.

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[2] A.N.Pudovik, J. Gen. Chem. 22, 462 (1952) (see C.B. translation, p. 521).

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Received June 2, 1950.

THE ADDITION OF DIALKYLPHOSPHOROUS ACIDS TO UNSATURATED COMPOUNDS

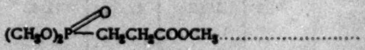
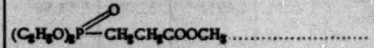
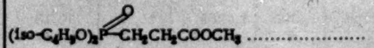
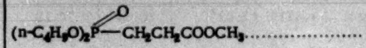
V. THE ADDITION OF DIALKYLPHOSPHOROUS ACIDS TO METHYL ACRYLATE, VINYL ACETATE, and VINYL BUTYL ETHER

A. N. Pudovik

As we have shown in a series of papers, the addition of dialkylphosphorous acids to unsaturated electronophilic reagents discovered by us may be employed as a simple and convenient method of synthesizing various ketophosphinic [1,3], cyanophosphinic [2], and carboxyalkylphosphinic esters, and unsaturated α-hydroxyphosphinic ethers [4]. The reaction takes place very readily in the presence of alcoholates of the alkali metals, the yields of the addition products being fairly high. Of the esters of α,β unsaturated carboxylic acids, the only one we have used for these reactions is methyl methacrylate. In the present paper we have made a study of the addition of dialkylphosphorous acids to methyl acrylate, vinyl butyl ether, and vinyl acetate by way of a more comprehensive and thoroughgoing study of the addition of dialkylphosphorous acids to esters of unsaturated carboxylic acids and to ethers of unsaturated alcohols, and to learn the effect of the structure of reagents upon their ability to enter into addition reactions.

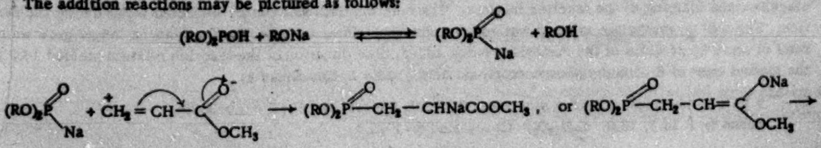
In connection with these presuppositions, it was found that the addition of dialkylphosphorous acids to methyl acrylate, which contains an unsubstituted vinyl group, is much more energetic than that to methyl methacrylate. The addition reactions were carried out by a procedure similar to that described in our preceding papers [1-4]. The addition of dimethylphosphorous, diethylphosphorous, diisobutylphosphorous, and dibutylphosphorous acids to methyl acrylate yielded the corresponding addition products, the methyl esters of β-dialkylphosphopropionic acid, whose constants, molecular refraction, and yields are listed in Table 1.

TABLE 1

No.	Formula	Boiling point (°C)	n_D^{20}	d_4^{20}	MR_D		Yield, %
					Found	Calculated	
1	 $(CH_3O)_2P(=O)-CH_2CH_2COOCH_3$	137-138° (10 mm)	1.4390	1.2170	42.36	42.43	73
2	 $(C_2H_5O)_2P(=O)-CH_2CH_2COOCH_3$	154-155 (14 mm)	1.4346	1.1241	51.97	51.66	84
3	 $(iso\text{-}C_4H_9O)_2P(=O)-CH_2CH_2COOCH_3$	172-174 (12 mm)	1.4400	1.0495	70.31	70.13	77
4	 $(n\text{-}C_4H_9O)_2P(=O)-CH_2CH_2COOCH_3$....................	183-186 (11 mm)	1.4416	1.0480	70.63	70.13	76

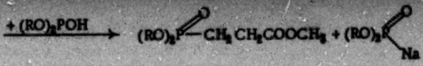
Saponifying the methyl ester of β-diethylphosphopropionic acid yielded β-phosphopropionic acid as minute crystals; their m.p. was 172-173° after having been dried in air. Nylen [5] gives the m.p. of β-phosphopropionic acid as 178°; α-phosphopropionic acid melts at 119-132° and deliquesces when left to stand in the air, according to Nylen [6] and A.E.Arbuzov and A.I. Razumov [7]. These findings on the saponification of the resultant addition products corroborate the formulas proposed for their structure as methyl esters of β-dialkylphosphopropionic acids.

The addition reactions may be pictured as follows:



$$(RO)_2POH + RONa \rightleftharpoons (RO)_2P(=O)Na + ROH$$

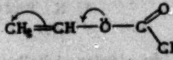
$$(RO)_2P(=O)Na + \overset{+}{C}H_2 = CH - C(=O^-)OCH_3 \longrightarrow (RO)_2P(=O)-CH_2-CHNaCOOCH_3, \text{ or } (RO)_2P(=O)-CH_2-CH=C(ONa)OCH_3 \longrightarrow$$



$$\xrightarrow{+ (RO)_2POH} (RO)_2P(=O)-CH_2CH_2COOCH_3 + (RO)_2P(=O)Na$$

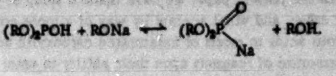
We then made a study of the addition of dialkylphosphorous acids to vinyl butyl ether and vinyl acetate. Vinyl butyl ether is a typical nucleophilic reagent, and as we have established, dialkylphosphorous acids are not added to this ether in the presence of alcoholates of the alkali metals. Nor were we able to effect this addition in the presence of protons (phosphoric acid), though carboxylic acids are added with great ease to vinyl ethers under analogous conditions, [8].

It might have been thought that vinyl acetate would be much more nucleophilic

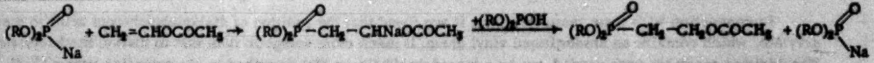


$$CH_2=CH-\ddot{O}-C(=O)CH_3 \qquad (a)$$

than electronophilic (a) and thus would be just as inert toward the addition of dialkylphosphorous acids. It was found, however, that the electronophilic nature of vinyl acetate is rather pronounced, as dialkylphosphorous acids are added to it quite energetically in the presence of alcoholates of the alkali metals. The addition obviously occurs directly at the carbon-carbon double bond and may be represented as follows:



$$(RO)_2POH + RONa \rightleftarrows (RO)_2P(=O)Na + ROH.$$



$$(RO)_2P(=O)Na + CH_2{=}CHOCOCH_3 \rightarrow (RO)_2P(=O)-CH_2-CHNaOCOCH_3 \xrightarrow{+(RO)_2POH} (RO)_2P(=O)-CH_2-CH_2OCOCH_3 + (RO)_2P(=O)Na$$

The constants, the molecular refraction values, and the yields of the resultant addition products — β-dialkylphosphoethyl acetates — are listed in Table 2.

TABLE 2

No.	Formula	Boiling point	n_D^{20}	d_4^{20}	MRD Found	MRD Calculated	Yield, %
1	$(CH_3O)_2P(=O)-CH_2CH_2OCOCH_3$	104-105° (5 mm)	1.4298	1.1882	42.59	42.43	72
2	$(C_2H_5O)_2P(=O)-CH_2CH_2OCOCH_3$	124-125° (9 mm)	1.4266	1.0214	51.33	51.66	57
3	$(iso\text{-}C_4H_9O)_2P(=O)-CH_2CH_2OCOCH_3$	147 (10 mm)	1.4325	1.0263	70.83	70.13	56
4	$(n\text{-}C_4H_9O)_2P(=O)-CH_2CH_2OCOCH_3$	143 (6 mm)	1.4312	1.0275	70.54	70.13	33

Saponification of β-diethylphosphoethyl acetate yielded β-hydroxyethylphosphinic acid as a viscous, straw-yellow oil. The acid did not crystallize even after long standing.

EXPERIMENTAL

Addition of dimethylphosphorous acid to methyl acrylate. A saturated solution of sodium methylate in methanol was slowly added, drop by drop, to a reaction mixture consisting of 11 g of dimethylphosphorous acid and 8.6 g of methyl acrylate, placed in a small Arbuzov flask. The reaction was extremely violent, with loud crackling and foaming of the reaction mixture. The reaction flask was cooled with cold water during the reaction. The sodium methylate solution was added a drop at a time until the reaction mass no longer grew warm, a total of some 20-25 drops of the methylate being added. Fractionation of the reaction mixture yielded 14.3 g of the methyl ester of β-dimethylphosphopropionic acid (Table 1, Compound 1).

0.1416 g substance: 0.0908 g substance: 39.5 ml, 26.9 ml NaOH (T = 0.019589).
Found %: P 15.8, 16.0. $C_6H_{13}O_5P$. Calculated %: P 15.7.

Addition of diethylphosphorous acid to methyl acrylate. 16 grams of diethylphosphorous acid and 10 g of methyl acrylate were used in the reaction in the presence of sodium ethylate, the procedure being the same as that described in the preceding experiment. Fractionation of the reaction mixture yielded 21.8 g of the methyl ester of β-diethyl-phosphopropionic acid (Table 1, Compound 2).

0.1240 g substance, 0.1342 g substance: 30.8 ml, 33.5 ml NaOH (T = 0.019589). Found %: P 13.5, 13.6. $C_8H_{17}O_5P$. Calculated %: P 13.8.

Saponification of the methyl ester of β-diethylphosphopropionic acid. 3.8 g of the ester was heated to 130-140° for 8 hours with 40 ml of 1:1 dilute hydrochloric acid. This yielded 2.2 g of ethyl chloride (2.1 g being called for theoretically). The hydrochloric acid was eliminated by repeated evaporation of the reaction mixture, with distilled water added after each evaporation. When the reaction mixture was evaporated to small volume, white crystals settled out, which had a m.p. of 172-173° after double recrystallization from water and drying in air.

0.1368 g substance: 50.3 ml NaOH (T = 0.019589). Found %: P 20.0. $C_3H_7O_5P$. Calc. %: P 20.1.

Addition of diisobutylphosphorous acid to methyl acrylate. The reaction was carried out with 14.6 g of diisobutylphosphorous acid and 6 g of methyl acrylate in the presence of sodium diisobutylate. The yield was 15.8 g of the methyl ester of β-diisobutylphosphopropionic acid (Table 1, Compound 3).

0.1022 g substance: 21.3 ml NaOH (T = 0.019589). Found %: P 11.3. $C_{12}H_{25}O_5P$. Calc.%: P 11.1.

Addition of dibutylphosphorous acid to methyl acrylate. A saturated solution of sodium butylate in butyl alcohol was added a drop at a time to a mixture of 8.3 g of dibutylphosphorous acid and 4 g of methyl acrylate. The reaction involved the evolution of considerable heat. A total of approximately 1 ml of the butylate solution was added. Fractionation of the reaction mixture yielded 9.4 g of the methyl ester of β-dibutylphosphopropionic acid (Table 1, Compound 4).

0.0944 g substance: 19.6 ml NaOH (T = 0.019589). Found %: P 11.4. $C_{12}H_{25}O_5P$. Calc.%: P 11.1.

Addition of dialkylphosphorous acids to vinyl acetate. 1. Addition of dimethylphosphorous acid. A saturated solution of sodium methylate in methanol was added very slowly, a drop at a time, to a reaction mixture consisting of 8.6 g of vinyl acetate and 11 g of dimethylphosphorous acid placed in an Arbuzov flask. The reaction caused the reaction mixture to warm up considerably; characteristic crackling was audible when the first few drops of the methylate were added. The sodium methylate was added until the reaction mixture did not heat up any longer, a total of about 20 drops being added in the course of 30 minutes. Fractionation of the reaction mixture yielded 14.1 g of β-dimethylphosphoethyl acetate (Table 2, Compound 1).

0.1312 g substance, 0.1284 g substance: 38.6 ml NaOH, 38.1 ml NaOH (T = 0.019589). Found %: P 16.0, 16.1. $C_6H_{13}O_5P$. Calculated %: P 15.7.

2. Addition of diethylphosphorous acid. 9 g of vinyl acetate and 13.1 g of diethylphosphorous acid were used for the reaction in the presence of sodium ethylate, which was carried out as specified above. Fractionation of the reaction mixture yielded 12.5 g of β-diethylphosphoethyl acetate (Table 2, Compound 2).

0.1160 g substance: 29.5 ml NaOH (T = 0.019589). Found %: P 13.8. $C_8H_{17}O_5P$. Calc.%: P 13.8.

3. Addition of diisobutylphosphorous acid. 4.3 g of vinyl acetate and 9.3 g of diisobutylphosphorous acid were used in this reaction, which was carried out in the presence of sodium isobutylate. The reaction was much quieter, with less heat evolved, than in the first two experiments. Fractionation of the reaction mixture yielded 7.6 g of β-diisobutylphosphoethyl acetate (Table 2, Compound 3).

0.1320 g substance: 27 ml NaOH (T = 0.019589). Found %: P 11.1. $C_{12}H_{25}O_5P$. Calc.%: P 11.1.

4. Addition of dibutylphosphorous acid. The reaction was carried out with 15 g of vinyl acetate and 11 g of dibutylphosphorous acid in the presence of sodium butylate. The yield was 9.5 g of β-dibutylphosphoethyl acetate (Table 2, Compound 4).

0.0944 g substance: 19.6 ml NaOH (T = 0.019589). Found %: P 11.4. $C_{12}H_{25}O_5P$. Calc.%: P 11.1.

SUMMARY

1. It has been shown that the dialkylphosphorous acids are added to methyl acrylate and vinyl acetate in the presence of alcoholates of the alkali metals, giving rise to the corresponding methyl esters of α,β-dialkylphosphopropionic acid and to β-dialkylphosphoethyl acetates.

2. The dialkylphosphorous acids are not added to vinyl butyl ether in the presence of alcoholates of the alkali metals or of phosphoric acid.

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[2] Ibid., J. Gen. Chem., 21, 1837 (1951).2)

[3] A.N. Pudovik. J. Gen. Chem., 22, 462 (1952).3)

[4] Ibid., J. Gen. Chem., 22, 467 (1952).4)

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Received June 2, 1950

The A.E.Arbuzov Institute of Chemistry of the
Kazan Branch of the USSR Academy of Sciences

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THE PHOTOREACTIONS OF ORGANOMETALLIC COMPOUNDS OF MERCURY IN SOLUTIONS

IX. THE REACTIONS OF p-DIANISYLMERCURY

Yu. A. Oldekop and N. N. Zolotareva

In our previous reports [1] we investigated the photoreactions of diphenyl-, dibenzyl-, o-ditolyl-, p-ditolyl-, α-dinaphthyl-, and dimesitylmercury in various organic solvents, finding certain general patterns of the behavior of the various radicals in photoreactions occurring in organic solvents. The organomercury compounds tested contained radicals of aromatic hydrocarbons, which possessed no functional groups, attached to the mercury. We were interested in testing the influence of substituents in the aromatic ring upon the progress of these photoreactions. The first example we chose was p-dianisylmercury, with carbon tetrachloride, chloroform, and methanol used as solvents. It was in these solvents that the most thoroughgoing investigation of the photoreactions of the other mercury derivatives had been made.

It is much harder to get a photoreaction of p-dianisylmercury than the reactions of the diaryl-substitutes of mercury tested previously. This is evidently due to the extremely sparing solubility of p-dianisylmercury in these organic solvents. p-Anisylmercury chloride and anisole were found in the reaction products of our tests in which chloroform was employed. This reaction may be pictured as follows. At first we have a dissociation into the p-anisyl and p-anisylmercury radicals:

$$(p\text{-}CH_3OC_6H_4)_2Hg + h\nu \rightarrow p\text{-}CH_3OC_6H_4Hg\cdot + p\text{-}CH_3OC_6H\cdot.$$

These radicals then react with the chloroform:

$$p\text{-}CH_3OC_6H_4Hg\cdot + CHCl_3 \rightarrow p\text{-}CH_3OC_6H_4HgCl + \cdot CHCl_2\,;$$

$$p\text{-}CH_3OC_6H_4\cdot + CHCl_3 \rightarrow CH_3OC_6H_5 + CCl_3\cdot.$$

It is seen that this photoreaction is quite similar to the reactions of Ar_2Hg in chloroform that we investigated previously. This analogy no longer applies, however, to the photoreaction in carbon tetrachloride, in which the end products are calomel, anisole, and a slight quantity of tarry products.

In our preceding papers we have shown that the phenyl and tolyl radicals detach chlorine from carbon tetrachloride, producing the corresponding chlorohydrocarbons and arylmercury chlorides. In the present instance, the radical does not react with the chlorine in the carbon tetrachloride, but detaches water from the methoxy group. We have often noticed reactions in which water is split off before chlorine is. The absence of these reactions in diphenylmercury is obviously attributable to the stability of the C–H bond in the benzene ring. It is therefore very highly likely that the hydrogen required for the formation of anisole comes from the CH_3- group rather than from the ring. A similar reaction was observed in the α-dinaphthylmercury: it is the second naphthyl radical in the α-naphthyl that yields naphthalene. This leads to the following set of reactions for p-dianisylmercury:

$$p\text{-}CH_3OC_6H_4Hg\cdot + CCl_4 \rightarrow p\text{-}CH_3OC_6H_4\cdot + HgCl + \cdot CCl_3;$$

$$2CH_3OC_6H_4\cdot \rightarrow CH_3OC_6H_5 + (CH_2OC_6H_4)_x.$$

The reaction was extraordinarily slow in methanol, probably due to the very sparing solubility of p-dianisylmercury in this solvent. But no tar was formed during the photoreaction, notwithstanding the extremely long exposure. The reaction products were found to contain anisole, mercury, and formaldehyde. All these substances could have been predicted from the reactions of Ar_2Hg with methanol investigated earlier, so that a reaction resembling that for the mercury derivative investigated previously may be advanced:

$$(p\text{-}CH_3OC_6H_4)_2Hg + CH_3OH \rightarrow 2CH_3OC_6H_5 + CH_2O + Hg.$$

These findings lead us to assert that a benzene ring containing the polar CH_3O- group exerted no major influence upon the course of the reaction, which is further evidence of the latter's radical nature. In ionic processes, the influence of the CH_3O-polar group ought to be very marked in the processes investigated.

EXPERIMENTAL

p-Dianisylmercury and carbon tetrachloride. 1.5 g of p-dianisylmercury was irradiated for 200 hours in 20 ml of carbon tetrachloride. The p-dianisylmercury was not fully dissolved in the carbon tetrachloride, so that the contents of the quartz test tube had to be vigorously shaken up from time to time. The reaction mass turned brown, with noticeable tarring.

After the reaction was over, the 0.92 g of the precipitate was filtered out. Hot benzene was used to extract from this precipitate 0.34 g of unreacted p-dianisylmercury, representing 22.7 % of the amount used for the reaction; its melting point proved to be 199°, exhibiting no depression when mixed with the known pure product. The substance that was insoluble in benzene proved to be calomel (blackened by concentrated ammonia) weighing 0.58 g or 68.2% of the theoretical.

The filtrate was distilled on a water bath, and the distillate was nitrated. The nitro product proved to be p-nitroanisole with a m.p. of 54°, exhibiting no depression when mixed with pure p-nitroanisole.

p-Dianisylmercury and chloroform. 1.5 g of p-dianisylmercury was irradiated for 17 hours in 20 ml of chloroform, the solution turning yellow. A precipitate settled to the bottom of the test tube; it was filtered out and recrystallized from acetone. The resultant substance had a m.p. of 239° and proved to be p-anisylmercury chloride, its mixed melting point with the pure preparation exhibiting no depression. The yield was 0.89 g or 71.7% of the theoretical.

The filtrate was distilled on a water bath; the distillate was nitrated, yielding p-nitroanisole with a m.p. of 54°, which exhibited no depression with the pure substance. The distillation residue was the unreacted p-dianisylmercury, which had a m.p. of 199° after recrystallization from benzene and exhibited no depression when mixed with the pure product. It weighed 0.3 g or 20.0% of the initial quantity.

p-Dianisylmercury and methanol. 1.5 g of p-dianisylmercury was irradiated for 540 hours in 20 ml of methanol, the contents of the test tube being vigorously shaken up from time to time. The reaction mass remained colorless despite the prolonged radiation time. Metallic mercury settled out on the bottom of the test tube and was separated from the unreacted p-dianisylmercury by dissolving the latter in benzene. This yielded 0.34 g of metallic mercury, equivalent to 47.2% of the theoretical, and 0.69 g of unreacted p-anisylmercury, or 46.0% of the initial quantity. Its melting point was 199° after it had been recrystallized from benzene, exhibiting no depression when mixed with known p-dianisylmercury.

The filtrate was distilled on a water bath, the distillate being diluted with water, and the anisole extracted with carbon tetrachloride and nitrated. The melting point of the nitro compound was 54° (from alcohol); it exhibited no depression when mixed with pure p-nitroanisole. The alcoholic solution contained formaldehyde (fuchsinsulfurous acid, silver mirror).

SUMMARY

1. When a solution of p-dianisylmercury in carbon tetrachloride is irradiated, calomel and anisole are formed as the result of the detaching of hydrogen from the methoxy group.

2. Irradiation of p-dianisylmercury in chloroform yields p-anisylmercury chloride and anisole.

3. The photoreaction of p-dianisylmercury in methanol yielded anisole, mercury, and formaldehyde, though the reaction was extremely slow owing to the sparing solubility of the mercury compound.

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Received May 22, 1950

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THE PHOTOREACTIONS OF ORGANIC COMPOUNDS OF MERCURY IN SOLUTIONS

X. THE REACTIONS OF DIMETHYLMERCURY

G.A.Razuvaev, Yu.A.Oldekop, and Z.N.Manchinova

In one of our previous papers [1] we cited the photoreaction of dimethylmercury with carbon tetrachloride, in which methylmercury chloride was produced. We have made a more thorough study of these reactions with diarylmercury derivatives. The reaction involves an initial dissociation of the organomercury compound into the RHg· and R· radicals.

After this paper of ours had appeared in print, several articles were published on the photoreactions of dimethylmercury. Gomer and Noyes [2], for example, investigated the photolysis of dimethylmercury at various temperatures and pressures. They took the initial process to be the formation of radicals, followed by a thermal reaction:

$$(CH_3)_2Hg \xrightarrow{h\nu} CH_3Hg\cdot + CH_3\cdot,$$

$$CH_3Hg\cdot \longrightarrow CH_3\cdot + Hg.$$

Ethane is formed by the collision of two methyl radicals or by the reaction of the methyl radical with dimethylmercury. In the latter case methane may also be produced by the detachment of hydrogen from a methyl radical of the dimethylmercury. Phibbs and de Darwent [3] made a study of the photoreaction of dimethylmercury with hydrogen in the gas phase, which takes place as follows:

$$(CH_3)_2Hg \xrightarrow{h\nu} 2CH_3\cdot + Hg,$$

$$CH_3\cdot + H_2 \rightarrow CH_4 + H\cdot,$$

$$H\cdot + (CH_3)_2Hg \rightarrow CH_4 + CH_3\cdot + Hg.$$

Ethane is formed in a side reaction:

$$CH_3\cdot + (CH_3)_2Hg \rightarrow C_2H_6 + Hg + CH_3\cdot,$$

$$2CH_3\cdot + M \rightarrow C_2H_6 + M.$$

At high temperatures the dimethylmercury is also decomposed thermally, a large part of the methyl radicals being "thermal".

Gomer [4] investigated the photo reaction of dimethylmercury with n-butane at 150-200°. The methyl radical initially formed during photolysis then reacted with the butane, detaching hydrogen from it:

$$CH_3\cdot + C_4H_{10} \rightarrow CH_4 + C_4H_9\cdot$$

But all these papers deal with research in the gas phase.

Bawn and Whitby [5] suggested that organometallic compounds of silver and copper, which decompose very readily at low temperatures, be employed in investigating the reaction of the methyl radical in solutions. But when we decompose methylsilver, all we get is ethane, no reaction with the solvent taking place; the decomposition of methylsilver does not polymerize styrene or methyl methacrylate. All this is indisputable evidence that no methyl radical is present during the decomposition of methylsilver, which evidently is of an ionic nature. Methylcopper causes the polymerization of the above-mentioned substances, but this process is due to copper ions rather than to radicals. Methylcopper reacts with alcohol when no air is present without forming any aldehyde, the reaction being apparently an ionic one.

$$CH_3Cu + CH_3OH \longrightarrow Cu^+ + CH_4 + CH_3O\cdot$$

The methyl radical may be secured in solutions by the Kharasch reaction [6], involving the addition of $CoCl_2$ or other metallic chlorides to organomagnesium chlorides. But this method requires the use of specific reaction conditions. The method of securing the methyl radical by decomposing acetyl peroxide in solutions is extremely convenient, the equation being:

$$CH_3COOOCOCH_3 \longrightarrow CH_3\cdot + CO_2 + \cdot OCOCH_3.$$

Very recently, [7], however, doubts have arisen whether methyl radicals are the initial product of the decomposition of the peroxide. It may be that the peroxide is dissociated into radicals as follows:

$$CH_3COOOCOCH_3 \longrightarrow 2\,CH_3CO_2,$$

yielding more highly stabilized alkoxy radicals, which then react with the solvent. Then the methyl radical is produced by the evolution of the CO_2 molecule.

That is why we believe that the photolysis of dimethylmercury is the most convenient reaction for investigating the behavior of methyl radicals in solutions.

The initial reaction is the detaching of one methyl group:

$$(CH_3)_2Hg \xrightarrow{h\nu} CH_3Hg\cdot + CH_3.$$

That a methylmercury radical has been formed is proved beyond the shadow of doubt by its reactions with halogen-containing solvents. Like an ArHg radical, the CH_3Hg radical detaches a halogen atom from the solvent. Thus, in experiments run in a carbon tetrachloride or chloroform solution, methylmercury chloride is produced, methylmercury iodide being formed in a methyl iodide solution. In solvents that contain no halogen, methylmercury breaks down further into mercury and a methyl radical.

In a methanol or chloroform solution the methyl radical reacts with hydrogen, giving rise to methane, formaldehyde being detected in the methanol solution and hexachloroethane in the chloroform solution. Thus, the outlines of the photoreactions for dimethylmercury remain the same as those we put forward earlier for Ar_2Hg.

When the dimethylmercury reaction is carried out in methyl iodide, methylmercury iodide is produced, as has been stated above. Thus two methyl radicals are set free: one from the dimethylmercury and the other from the methyl iodide. We might, therefore, expect ethane to be formed:

$$CH_3HgCH_3 + ICH_3 \longrightarrow CH_3HgI + C_2H_6.$$

The gas evolved in the reaction is methane, however. Hence, the methyl radicals react with the solvent, detaching hydrogen from it; thus this reaction is similar to the one described for the photoreaction of diphenylmercury with methyl iodide in a methanol solution [8]. Only when the photoreaction of dimethylmercury was carried out in a carbon tetrachloride solution was no methane formed. In this case, the methyl radical reacted by detaching a chlorine atom from the solvent, producing methyl chloride.

It is worthy of note that the methyl radicals do not detach hydrogen from benzene or 2,2,4-trimethylpentane under the conditions we have described, metallic mercury and ethane being produced in photoreactions in these solvents. The reactions are much harder to carry out than in other solvents. When dimethylmercury is irradiated in a solution consisting of a methanol– carbon tetrachloride mixture, the methyl mercury and methyl radicals formed at the start of the reaction react with different constituents of the solvent. The equations for the reaction are:

$$CH_3Hg\cdot + CCl_4 \longrightarrow CH_3HgCl + CCl_3\cdot\,,$$

$$2CCl_3\cdot \longrightarrow Cl_3CCCl_3,$$

$$2\,CH_3\cdot + CH_3OH \longrightarrow 2CH_4 + CH_2O.$$

This experiment proves that the methyl radicals must exist in the solution for some time, reacting selectively.

EXPERIMENTAL

Dimethylmercury and methanol. A solution of 1.5 g of dimethylmercury in 20 ml of methanol was placed in a quartz test tube connected to a gas buret and irradiated with a mercury quartz lamp for 40 hours. Gas was evolved during the reaction, 215 ml being collected. Gas analysis indicated that the gas was methane. The evolution of metallic mercury in the photolysis of the dimethylmercury during the reaction was highly interesting: the mercury settled out continuously as extremely small drops on the bottom of the test tube, so that a substantial drop of mercury had accumulated on the test-tube bottom by the end of the reaction. The drop was filtered out; it weighed 1.0 g (76% of the theoretical yield). Formaldehyde was found in the filtrate (dimedon derivative with a m.p. of 189°).

Dimethylmercury and 2,2,4-trimethylpentane. A solution of 1.5 g of dimethylmercury in 7 ml of 2,2,4-trimethylpentane was irradiated for 30 hours, during which time 63 ml of a gas that proved to be ethane was collected. The metallic mercury produced during the reaction was filtered out; it weighed 0.55 g, equivalent to 42% of the theoretical.

Dimethylmercury and benzene. 1.5 g of dimethylmercury was irradiated in 20 ml of benzene for 40 hours, 37 ml of gas being collected during this time. Analysis indicated that the gas was ethane. The metallic mercury that settled out during the reaction was filtered out; it weighed 0.4 g, equivalent to 31% of the theoretical.

Dimethylmercury and chloroform. A solution of 1.5 g of dimethylmercury in 7 ml of chloroform was irradiated for 60 hours, during which time 120 ml of gas was collected. Gas analysis indicated that the gas was methane. A white crystalline substance with a slight gray coating of metallic mercury formed inside the test tube. The precipitate was filtered out and recrystallized from dichloroethane (m.p. 170°), exhibiting no depression with pure methylmercury chloride. The filtrate was distilled with steam, a white crystalline substance with the odor of camphor solidifying in the condenser. It had a m.p. of 184° (in a sealed capillary) after having been sublimed over concentrated sulfuric acid, exhibiting no depression of the melting point when mixed with pure hexachloroethane Distillation of the residue yielded some more methylmercury chloride, the aggregate weight of methylmercury chloride being 1.35 g, or 83% of the theoretical.

Dimethylmercury and methyl iodide. A solution of 1.5 g of dimethylmercury in 7 ml of methyl iodide was irradiated for 50 hours, 132 ml of gas being collected during that time. Gas analysis proved that the gas was methane. The precipitate formed during the reaction was filtered out; traces of metallic mercury and mercuric iodide were visible in it. The precipitate was recrystallized from alcohol (m.p. 145°), exhibiting no depression of the melting point with pure methylmercury chloride. The filtrate was distilled, the residue consisting of methylmercury chloride, with a m.p. of 145°, the total weight of the latter compound being 1.9 g, or 85% of theory.

Dimethylmercury and carbon tetrachloride. 1.5 g of dimethylmercury in 3 ml of carbon tetrachloride was irradiated for 50 hours. The precipitate (in which traces of mercury were observed) was filtered out and recrystallized from dichloroethane (m.p. 170°), exhibiting no depression of the melting point when mixed with pure methylmercury chloride. During the experiment, 8 ml of gas was collected and dissolved in methanol. This solution yielded a precipitate of silver chloride when allowed to stand with a solution of silver nitrate. No methane was found.

The filtrate was distilled, hexachloroethane solidifying in the condenser; the hexachloroethane was extracted and sublimed over sulfuric acid; its m.p. was 184°, exhibiting no depression when mixed with the pure preparation. The residue contained methylmercury chloride (m.p. 170°), exhibiting no depression of the melting point when mixed with the pure product. The total weight of methylmercury chloride was 1.3 g, or 80% of the theoretical yield.

Dimethylmercury in methanol and carbon tetrachloride. A solution of 1.5 g of dimethylmercury in 3 ml of methanol and 3 ml of carbon tetrachloride was irradiated for 40 hours, 80 ml of gas being collected during that time Analysis proved that the gas was methane. The crystalline precipitate, which contained traces of metallic mercury, was filtered out and recrystallized from alcohol (m p. 170°); the mixed melting point with pure methylmercury chloride exhibited no depression. The precipitate weighed 0.8 g, or 50% of the theoretical. The filtrate was distilled, formaldehyde being found in the distillate (dimedon derivative with a m.p. of 189°). Hexachloroethane (m p. 184°) was extracted from the condenser, its mixed melting point with the pure product exhibiting no depression.

SUMMARY

1. It has been proved that dimethylmercury is broken down by photolysis into the $CH_3^\bullet$ and $CH_3Hg^\bullet$ radicals; the reaction is the same as that for the aryl compounds of mercury.

2. Dimethylmercury reacts with methanol when irradiated by ultraviolet light, yielding methane, mercury, and formaldehyde.

3. The photoreaction of dimethylmercury with chloroform yields methylmercury chloride, methane, and hexachloroethane.

4. When dimethylmercury is irradiated in methyl iodide solution, it yields methylmercury chloride and methane.

5. Irradiation of dimethylmercury dissolved in carbon tetrachloride yields methylmercury chloride, methyl chloride, and hexachloroethane.

6. When the photoreaction is carried out with dimethylmercury dissolved in methanol and carbon tetrachloride, photolysis yields the $CH_3Hg^\cdot$ and methyl radicals, which react with different components of the solution. The first radical reacts with the carbon tetrachloride, yielding methylmercury chloride, while the methyl radical reacts with the methanol to yield methane.

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Received June 28, 1950. Gorky State University

THE REACTION OF DIPHENYLMERCURY WITH METALLIC CHLORIDES THAT DO NOT FORM STABLE ORGANOMETALLIC COMPOUNDS

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The radical – halogen reaction is a general reaction for organoelemental compounds of considerable practical interest, inasmuch as it makes possible the synthesis of any organoelemental compound. Organometallic compounds of mercury may be used successfully for this purpose, particularly when we have to synthesize an organoelemental compound containing functional groups. The reaction of organomercury compounds with halogen derivatives was used to prepare organic compounds of boron, thallium, silicon, tin, phosphorus, arsenic, antimony, bismuth, and iodine [1].

When metallic halides, which do not form organometallic compounds, are used in the reaction, the course of the reaction changes sharply. The changes produced in the reactions of organomagnesium and organolithium compounds by the addition of slight amounts of cobalt, iron, and manganese, due to the formation of unstable organometallic compounds that then break down, yielding free radicals:

$$RMgCl + CoCl_2 \longrightarrow RCoCl + MgCl_2;\ RCoCl \longrightarrow R^{\cdot} + CoCl^{\cdot},$$

have been investigated in the greatest detail [2].

Recently some organocobalt compounds have been produced in a Grignard reaction from cobalt chloride [3]. The singular chemical reactions of organomagnesium and organolithium compounds are also explainable by the ensuing processes brought about by the $R^{\cdot}$ and $CoCl^{\cdot}$ radicals.

We felt it would be of interest to check the course of the reactions with cobaltous, ferric, and cupric chlorides, as well as with other organometallic compounds, in order to determine how far these processes are common to them all. We confined ourselves to organomercury compounds and have already noted many examples of reactions that involve a stage in which free radicals are formed [4]. Diphenylmercury often reacts with dissociation into radicals:

$$(C_6H_5)_2Hg \longrightarrow C_6H_5Hg^{\cdot} + C_6H_5^{\cdot}.$$

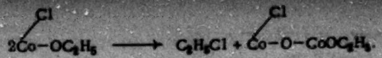
Characteristic of the phenyl radical are the reactions in which it is saturated with hydrogen, coming from the solvent. When alcoholic solutions of diphenylmercury are heated, for example, the phenyl radical reacts with the alcohol, yielding benzene and an aldehyde [5]. The photoreactions of diphenylmercury with alcohols, ethylcellosolve [6], dioxane [7], and morpholine are like the preceding ones. In every case the phenyl radical is converted into benzene by detaching hydrogen from the solvent.

In the present research we have investigated the reaction of diphenylmercury with cobaltous chloride, ferric chloride, and cupric chloride in solutions of ethylcellosolve, dioxane, and morpholine. When anhydrous cobaltous chloride is added to a heated solution of diphenylmercury in ethylcellosolve and the mixture is cooled, crystals of phenyl mercury chloride and of a cobalt compound settle out. Benzene and acetaldehyde were found in the ethylcellosolve solution. The phenylmercury chloride was removed from the precipitate by treating the latter with dichloroethane, the residue consisting of the cobalt compound, which was insoluble in water, though readily soluble in acids. Cobalt hydroxide was precipitated from the acid solution by an alkali, part of the solution was driven off, the presence of ethyl alcohol in the distillate being proved by an iodoform test. A chlorine content equivalent to one chlorine atom to two cobalt atoms was proved in the resultant compound. It was thus found that the reaction involves the splitting of one phenyl radical out of the diphenylmercury, the radical reacting with the solvent, ethylcellosolve, to produce benzene and acetaldehyde. The reaction may be pictured as follows:

$$(C_6H_5)_2Hg + CoCl_2 \rightarrow C_6H_5HgCl + C_6H_5CoCl;\ C_6H_5CoCl \rightarrow C_6H_5^{\cdot} + CoCl^{\cdot};$$

$$HOCH_2CH_2OC_2H_5 + C_6H_5^{\cdot} + CoCl^{\cdot} \longrightarrow C_6H_6 + CH_3CHO + ClCoOC_2H_5.$$

The composition of the resultant cobalt derivatives was close to that given by the formula $Co_2ClO_2C_2H_5$, however. The formation of this compound may be hypothetically represented by the following equation:



$$2\overset{Cl}{Co}-OC_2H_5 \longrightarrow C_2H_5Cl + \overset{Cl}{Co}-O-CoOC_2H_5.$$

The reaction of diphenylmercury with ferric chloride in an ethylcellosolve solution is simpler. The reaction yielded phenylmercury chloride, benzene, acetaldehyde, and ferrous chloride:

$$(C_6H_5)_2Hg + FeCl_3 \rightarrow C_6H_5HgCl + FeCl_2 + C_6H_5^{\cdot}. \qquad 2C_6H_5^{\cdot} + HOCH_2CH_2OC_2H_5 \rightarrow 2C_6H_6 + 2CH_3CHO.$$

The reaction with cupric chloride was altogether different, yielding phenylmercury chloride, chlorobenzene, and cuprous chloride:

$$(C_6H_5)_2Hg + 2CuCl_2 \longrightarrow C_6H_5HgCl + C_6H_5Cl + 2CuCl.$$

Thus this involved reaction of the phenyl radical with the solvent.

The reactions of diphenylmercury dissolved in dioxane are similar. The reaction with cobaltous chloride is greatly hampered by its sparing solubility in dioxane. Prolonged heating of the reaction mixture yielded phenylmercury chloride and benzene. Hence, here, too, the phenyl radical reacted with solvent, detaching hydrogen from the latter and turning into benzene:

$$(C_6H_5)_2Hg + CoCl_2 \rightarrow C_6H_5HgCl + C_6H_5CoCl; \qquad C_6H_5CoCl \rightarrow C_6H_5^{\cdot} + CoCl;$$

$$C_6H_5^{\cdot} + C_4H_8O_2 \longrightarrow C_6H_6 + C_4H_7O_2^{\cdot}.$$

We were unable to find any other reactions of the $CoCl^{\cdot}$ and $C_4H_7O_2^{\cdot}$ radicals. The photoreactions of diphenylmercury with dioxane yielded bidioxanyl, formed by the dimerization of the dioxanyl radicals. We found no bidioxanyl in our experiments, however.

Diphenylmercury reacts extremely readily with ferric chloride. Even gentle heating results in detachment of one phenyl radical and formation of phenylmercury chloride and ferrous chloride:

$$(C_6H_5)_2Hg + FeCl_3 \rightarrow C_6H_5HgCl + FeCl_2 + C_6H_5^{\cdot}; \qquad C_6H_5^{\cdot} + C_4H_8O_2 \rightarrow C_6H_6 + C_4H_7O_2^{\cdot}.$$

Nor were we able to find out what happened to the dioxane radical in this case either.

Cupric chloride dissolved in dioxane reacted exactly as it had in ethylcellosolve, i.e., phenylmercury chloride, chlorobenzene, and cuprous chloride were produced. The solvent played no part in the reaction.

The differences between the reactions of diphenylmercury with ferric chloride and cobaltous chloride, on the one hand, and with cupric chloride, on the other, in ethylcellosolve and dioxane solutions dissapear when the reactions are carried out in a morpholine solution. Benzene is formed and metallic mercury is thrown down in every case. In our test with cobaltous chloride we also found, in addition to the mercury, some phenylmercury chloride. It must be supposed that the reaction in morpholine follows a different course from the reactions described above.

Metallic halides form complex salts with morpholine; when the dark-green solution of cupric chloride in morpholine is heated, it turns colorless as the complex cupric salt is changed into a cuprous one [8]. As the colorless solution cools, considerable atmospheric oxygen is absorbed, and the dark-green coloration reappears. When cuprous chloride is dissolved in morpholine and the solution is heated, a colorless solution results, which absorbs oxygen as it cools and turns green. The same phenomenon is observed when diphenylmercury is present. The precipitation of mercury and the formation of benzene must be attributed to reduction reactions that occur as a solution of complex salts is heated. The absorption of atmospheric oxygen involves thoroughgoing oxidation of the morpholine, yielding large quantities of carbon dioxide, which is added to the morpholine to yield the volatile morpholine carbonate that we found in the reaction products.

EXPERIMENTAL

1. Reaction of diphenylmercury with ethylcellosolve and cobaltous chloride. 5.0 g of $(C_6H_5)_2Hg$ was dissolved in 40 g of ethylcellosolve, 2.0 g of anhydrous $CoCl_2$ was added to the solution, and the reaction mixture was refluxed for 3 hours. As it cooled, the crystalline precipitate that settled was filtered out. The precipitate consisted of phenylmercury chloride and a cobalt compound; they were separated by processing the precipitate with hot dichloroethane, in which the phenylmercury chloride dissolved. 3.3 g of a pure product with a m.p. of 254° was thrown down from the dichloroethane solution. Its mixed melting point with pure phenylmercury chloride exhibited no depression. After the phenylmercury chloride had been extracted, there remained a light-violet powder of a cobalt compound, which was insoluble in water, but dissolved readily in mineral acids.

Found %: Co 53.65; Cl 17.86, 17.66. $Co_2ClO_2C_2H_5$. Calculated %: Co 54.99; Cl 16.54.

The cobalt was precipitated from the acid solution with alkali, the cobalt hydroxide being filtered out, and part of the solvent being evaporated from the filtrate. The distillate was proved to contain ethyl alcohol by means of an iodoform reaction. The filtered liquid portion of the reaction mixture was then distilled. The initial fraction, distilling up to 110°, was diluted with water, yielding 1.4 g of benzene, which was nitrated to m-dinitrobenzene with a m.p. of 88°, exhibiting no depression when mixed with the pure substance. The presence of the aldehyde in the aqueous solution was proved by means of the usual reactions; the dimedon derivative of acetaldehyde had a m.p. of 140°.

2. Reaction of diphenylmercury with ethylcellosolve and ferric chloride. 2.3 g of anhydrous $FeCl_3$ was added to 5.0 g of $(C_6H_5)_2Hg$ dissolved in 38.0 g of ethylcellosolve, and the mixture was refluxed for 1 hour. As the mixture cooled, crystals of phenylmercury chloride settled out. The yield was 4.0 g of phenylmercury chloride (90.6% of the theoretical) with a m.p. of 252°, plus 1.3 g of benzene, from which m-dinitrobenzene with a m.p. of 90° was prepared. After the benzene had been removed, the aqueous solution yielded the dimedon derivative of acetaldehyde with a m.p. of 139-140°.

All these melting points were checked by the mixed melting points with the pure substances, no depression being found. The ferrous chloride was identified by the formation of Turnbull's blue.

3. Reaction of diphenylmercury with ethylcellosolve and cupric chloride. 2.0 g of anhydrous $CuCl_2$ was heated in 30.0 g of ethylcellosolve until it dissolved, and 5.0 g of $(C_6H_5)_2Hg$ was added to the solution while it was still warm. Some time later cuprous chloride was precipitated from the reaction mixture, and the solution was decolorized. Then the reaction mixture was refluxed for 5-10 minutes on a water bath. As it cooled, crystals of phenylmercury chloride settled on top of the cuprous chloride precipitate. The precipitates were filtered out and processed in the usual manner. The liquid portion was distilled with steam, a layer of chlorobenzene separating from the distillate. This yielded 3.9 g of phenylmercury chloride (88.3% of the theoretical) with a m.p. of 254°, and 1.55 g of chlorobenzene (97.5% of the theoretical), from some samples of which we prepared p-nitrochlorobenzene with a m.p. of 83° and 1,2,4-chlorodinitrobenzene with a m.p. of 50°. All these melting points were checked by mixing the products with known substances, no depression being found. The cuprous chloride was identified by the usual reactions.

4. Reaction of diphenylmercury with dioxane and cobaltous chloride. 2.0 g of anhydrous $CoCl_2$ was added to 5.0 g of $(C_6H_5)_2Hg$ in 20.0 g of dioxane. The cobaltous chloride was sparingly soluble in the dioxane, which slowed down the reaction. The mixture was refluxed for 3.5 hours. As it cooled, phenylmercury chloride settled down upon the precipitate of a light-violet cobalt compound. The precipitates were filtered out, and the phenylmercury chloride was extracted as described above. The filtrate was distilled with steam, a benzene layer separating out from the distillate. This yielded 1.0 g of phenylmercury chloride (22.6% of the theoretical) with a m.p. of 254.5° and 0.35 g of crude benzene (31.7% of the theoretical), from which we prepared m-dinitrobenzene with a m.p. of 89°. The mixed melting points of both of these products with the pure substances exhibited no depression. We did not analyze the cobalt compound.

5. Reaction of diphenylmercury with dioxane and ferric chloride. 5.0 g of $(C_6H_5)_2Hg$ was added to 2.0 g of $FeCl_3$ in 20.0 g of dioxane. A reddish-brown precipitate settled out as soon as the flask was heated gently. The mixture was refluxed for 30 minutes. After it had cooled, the precipitate was filtered out, and the phenylmercury chloride was extracted from it in the usual manner. Benzene separated from the distillate when the liquid portion was distilled with steam. This yielded 3.8 g of phenylmercury chloride (86.1% of the theoretical) with a m.p. of 255°, and 1.45 g of crude benzene, which yielded m-dinitrobenzene with a m.p. of 90°. The mixed melting points of the phenylmercury chloride and the m-dinitrobenzene with pure samples of these substances exhibited no depression. The ferrous chloride was identified by the production of Turnbull's blue.

6. Reaction of diphenylmercury with dioxane and cupric chloride. 2.0 g of anhydrous $CuCl_2$ was added to 5.0 g of $(C_6H_5)_2Hg$ in 24.0 g of dioxane. A white precipitate of cuprous chloride began to settle out even when the mixture was stirred at room temperature. The solution was refluxed for 10 minutes. As it cooled, crystals of phenylmercury chloride settled down upon the white precipitate of cuprous chloride. The precipitates were filtered out, the phenylmercury chloride being extracted in the usual manner. The liquid portion was distilled with steam. When the condensate was diluted with water, a layer of chlorobenzene settled out. This yielded 1.6 g of phenylmercury chloride (36.2% of the theoretical) with a m.p. of 255° and 0.75 g (47.2% of the theoretical) of crude chlorobenzene with a b.p. of 130-131° (by the Sivolobov method). The latter yielded 2,4-dinitro-1-chlorobenzene with a m.p. of 52° (from alcohol). The mixed melting points of both products with pure samples of these substances exhibited no depression.

7. Reaction of diphenylmercury with morpholine and cobaltous chloride. 2.0 g of anhydrous $CoCl_2$ was

added to 5.0 g of $(C_6H_5)_2Hg$ in 25.5 g of morpholine, and the solution was refluxed for 1 hour. Phenylmercury chloride settled out as the solution cooled. The precipitate was filtered out, and the phenylmercury chloride was separated from the cobalt compound in the usual manner. Distillation of the filtrate yielded a fraction passing over up to 110°, from which a benzene layer separated when it was diluted with water. Free mercury was also detected among the reaction products. This yielded: 0.4 g of phenylmercury chloride with a m.p. of 253° (from acetone), 0.35 g of crude benzene, from which we prepared m-dinitrobenzene with a m.p. of 90°, and 0.8 g of mercury. The mixed melting points of the m-dinitrobenzene and the phenylmercury chloride exhibited no depression when mixed with the pure products.

8. Reaction of diphenylmercury with morpholine and ferric chloride. 2.0 g of $FeCl_3$ was dissolved in 18.0 g of morpholine, the dissolution being very violent, with the evolution of considerable heat. Then 5.0 g of $(C_6H_5)_2Hg$ was added to the solution, and the whole was refluxed for 3 hours. A gray incrustation of metallic mercury separated out during heating. The contents of the flask crystallized upon cooling. The tarry liquid portion of the reaction mixture was decanted and distilled with steam, a layer of benzene appearing in the condensate. The tarry residue was dissolved in dilute hydrochloric acid, metallic mercury settling on the bottom of the flask. This yielded 0.87 g of mercury (30.8% of the theoretical) and 0.77 g of benzene (34.9% of the theoretical), from which we prepared m-dinitrobenzene with a m.p. of 90°. The mixed melting point of the latter compound exhibited no depression with a pure sample. No phenylmercury chloride was found.

9. Reaction of diphenylmercury with morpholine and cupric chloride. 2.0 g of anhydrous $CuCl_2$ was added to 5.0 g of $(C_6H_5)_2Hg$ in 18.0 g of morpholine, and the mixture was refluxed for 3 hours. As the solution was heated, its dark-green color disappeared, but reappeared upon cooling. Metallic mercury settled on the bottom of the flask. After the solution had cooled, it was decanted from the mercury and distilled with steam, a benzene layer separating from the condensate. This yielded 1.4 g of benzene (63.5% of the theoretical), from which we prepared m-dinitrobenzene with a m.p. of 88°. Its mixed melting point with a pure sample exhibited no depression. In addition, we secured 2.4 g of metallic mercury (84.9% of the theoretical).

From the reaction products of diphenylmercury with morpholine we isolated a substance that partially sublimed, and crystallized from the individual fractions (during fractionation of the liquid portion of the reaction product) as well as from the aqueous solutions after the benzene had been eliminated. It sublimed readily; m.p. 115° (in a sealed capillary); it was freely soluble in water, and sparingly so in benzene. It dissolved violently in dilute acids (HCl), giving off CO_2 and yielding morpholine hydrochloride with a m.p. of 174°. Its mixed melting point with the salt prepared from pure morpholine exhibited no depression. Reacting it with methyl iodide yielded morpholine methiodide:

Found %: I 55.36, 54.04. $C_5H_{12}NOI$. Calculated %: I 54.16.
Found %: H 8.12, 8.26; C 49.20, 49.00; N 12.89, 12.82; $C_9H_{18}O_4N_2$. Calculated %: H 8.26; C 49.50; N 12.83.

The analysis and properties of this substance indicated that it was morpholine carbonate, which was borne out by the preparation of the carbonate by reacting CO_2 with morpholine. The carbonate sublimed readily and fused at 114-115° in a sealed capillary.

SUMMARY

1. When a solution of diphenylmercury in ethylcellosolve or dioxane is heated with cobaltous chloride or ferric chloride, it yields phenylmercury chloride and benzene, due to the reaction of the phenyl radical with the solvent.

2. When a solution of diphenylmercury in ethylcellosolve or dioxane is heated with cupric chloride, the reaction yields phenylmercury chloride, chlorobenzene, and cuprous chloride.

3. When a solution of diphenylmercury in morpholine is heated with ferric chloride, cupric chloride, or cobaltous chloride, benzene is formed and metallic mercury is thrown down. The reaction probably involves reducing processes that occur when complex salts of metallic chlorides and morpholine are heated.

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Received May 22, 1950.

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THE SYNTHESIS AND THE POLYMERIZABILITY OF RING-HALOGENATED DERIVATIVES OF STYRENE

SYNTHESIS OF RING-DICHLORINATED STYRENES

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There are not many papers in the literature on the synthesis and properties of the dichlorostyrenes [1]. Of all the possible isomers of the dichlorostyrenes, it is the synthesis of 3,4-dichlorostyrene that is described in greatest detail [2], though a method of synthesis is given for 2,5-dichlorostyrene that starts out with materials that are extremely difficult to procure. We have endeavored to make a study of the synthesis of the dichlorostyrenes and to find a general method of preparing the isomeric dichlorostyrenes, viz., 2,4-dichlorostyrene; 2,5-dichlorostyrene; and 3,4-dichlorostyrene.

EXPERIMENTAL

I. Synthesis of 2,5-Dichlorostyrene

1. Preparation of 2,5-dichloroacetophenone. 168.0 grams of p-dichlorobenzene was mixed with 308.0 g of anhydrous aluminum chloride, and 180.0 g of acetyl chloride was added. The mixture was heated to 130° on an oil bath for 3 hours. The reaction mixture was decomposed by pouring ice and dilute HCl over the mixture, after which it was extracted with CCl_4, washed with 10% alkali and with water, and dried. The CCl_4 was driven off, and the residue fractionated in vacuo. 2,5-Dichloroacetophenone has a b.p. of 104-105° at 2 mm and 245-247° at atmospheric pressure; its m.p. is 9-10°. The yield was 102.0 g, or 46% of the theoretical.

2. Preparation of 2,5-dichlorophenylmethylcarbinol. 50.0 g of 2,5-dichloroacetophenone was dissolved in 350 ml of isopropyl alcohol, 75 ml of a solution of aluminum alcoholate was added, and the whole was heated on a water bath for 6 hours. This drove off all the acetone formed and a large part of the isopropyl alcohol. The residue was chilled with ice, acidulated with 10% HCl, extracted with benzene, washed, and dried, after which the benzene was driven off, and the residue was fractionated in vacuo, yielding 42.0 g of 2,5-dichlorophenylmethylcarbinol (84% of the theoretical) with a b.p. of 117° at 2 mm and a m.p. of 60-62°.

3. Synthesis of 2,5-dichlorostyrene. 2,5-Dichlorostyrene was synthesized, with a yield that was 50-60% of the theoretical, by dehydrating 2,5-dichlorophenylmethylcarbinol above Al_2O_3 at 350-400° and 120 mm mercury column. 2,5-Dichlorostyrene is an aromatic, colorless liquid (with the odor of styrene); its b.p. is 92-94° at 5 mm and 72-73° at 2 mm; its specific gravity at 20° is 1.246. It is readily polymerized.

II. Synthesis of 2,4-Dichlorostyrene

The 2,4-dichlorostyrene was synthesized by the same procedure as that used for the synthesis of the 2,5-dichlorostyrene, but starting out with m-dichlorobenzene. The yield of 2,4-chloroacetophenone, with a b.p. of 122-124° (12 mm) was 50% of the theoretical. The 2,4-dichloroacetophenone was reduced to a carbinol, the yield being 60% of the theoretical. The b.p. of 2,4-dichlorophenylmethylcarbinol was 126-128° (7 mm). Dehydrating the 2,4-dichlorophenylmethylcarbinol yielded 2,4-dichlorostyrene, the yield being 30% of the theoretical.

2,4-Dichlorostyrene is a colorless, aromatic liquid with a b.p. of 80-81° at 6 mm and a specific gravity of 1.249 at 20°. It is readily polymerized.

III. Synthesis of 3,4-Dichlorostyrene

The conditions used in synthesizing 3,4-dichlorostyrene were the same as those employed for 2,5-dichlorostyrene, but o-dichlorobenzene was employed as the initial material. The yield of 3,4-dichloroacetophenone, with a b.p. of 135° (12 mm) and a m.p. of 74°, was 64.5% of the theoretical. Reducing the

3,4-dichloroacetophenone gave us 73% of the theoretical yield of 3,4-dichlorophenylmethylcarbinol, with a b.p. of 126-127° (2 mm) and a specific gravity of 1.311 at 20°. Dehydrating the 3,4-dichlorophenylmethylcarbinol produced 75% of the theoretical yield of 3,4-dichlorostyrene.

3,4-Dichlorostyrene is a colorless, aromatic liquid with a b.p. of 92° at 6 mm and a specific gravity of 1.256 at 20°. It is harder to polymerize than the 2,5- and 2,4-dichlorostyrene.

SUMMARY

A general method has been developed for synthesizing 2,5-dichlorostyrene, 2,4-dichlorostyrene, and 3,4-dichlorostyrene.

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Received June 17, 1950

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ISOMERIZATION OF SALTS OF CINNAMYLIDENEANILINE

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The so-called "Schiff's bases" are not always basic. Many compounds of the ArCH=NAr type, whose amine rings contain electronegative substituents, do not manifest the slightest tendency to salt formation and are actually insoluble in acids. Yet, some of them are weakly basic, forming unstable addition products with strong acids. Lastly, fairly stable salts may be secured in some cases, able to stand recrystallization even from boiling water.

Reference is made in the chemical literature to the high stability of the addition product of hydrogen chloride to cinnamylideneaniline, which is mentioned, more particularly, by Izmailsky [1].

This salt, $C_6H_5CH=CH-CH=N-C_6H_5 \cdot HCl$, is readily prepared by the direct action of strong hydrochloric acid upon the freshly prepared anil, followed by recrystallization of the reaction product from hot water. As the aqueous solution cools, beautiful golden-yellow needles with a m.p. of 147-148° settle out (we have found the m.p. of this substance to be 151-152°).

Synthesizing the analogous salt of orthomethylcinnamylideneaniline (m.p. 93-95°) from orthotoluidine, we observed an appreciable difference in the behavior of these salts and in their external qualities. The anil salt had a lighter, golden "quinone" color and reacted less readily with a soda solution, whereas the salt of the orthomethyl anil could be crystallized from hot water only with a poorer yield, due to its pronounced hydrolysis into its original constituents, as is highly characteristic of many anil salts. This led us to suppose that the anil is not the primary reaction product, but rather the end product of some transformation occurring during heating or recrystallization. As a matter of fact, when freshly prepared cinnamylideneaniline was triturated with a slight excess of hydrochloric acid (sp.gr. 1.19) at room temperature, we secured an orange-colored mass, which had a m.p. of 80-82° after it had been carefully washed with water and dried on the filter. The substance greatly resembled the salt of orthomethylcinnamylidene. It reacted vigorously with a soda solution, was much more soluble in water than the substance with a m.p. of 151-152°, threw down a pronounced precipitate with $AgNO_3$, and behaved like a typical salt in all other respects. The compound displayed a positive double-bond reaction with permanganate.

It may well be that the most interesting property of this substance is its instability. It is transformed into the substance with a m.p. of 151-152° within the space of about 24 hours. This is why the low-melting salt was not detected by previous investigators, it being completely transformed into the high-melting product when recrystallized from hot water.

We have been able to observe this transition directly, utilizing the differing solubilities of the salts in water. This was done by placing a test tube containing an aqueous solution of the low-melting form saturated in the cold in a beaker of water. As the beaker was slowly heated on a water bath at 55°, the contents of the test tube quickly turned cloudy, throwing down crystals of another, less soluble form, which redissolved as heating was continued; when the solution was cooled, nothing but the substance with a m.p. of 151-152° settled out.

The paramethylanil yielded different results: no matter what experimental conditions were employed, the only salt it yielded was one with a m.p. of 168-170°, whose properties greatly resembled those of the high-melting anil salt, especially in its being able to stand recrystallization from hot water without suffering any change in its properties or its melting point. The salt of the paramethylanil exhibits no tendency toward conversion into another form.

We also found that the property of forming two kinds of salts is not peculiar to cinnamylideneaniline. Our experimental data are listed in the following table.

TABLE

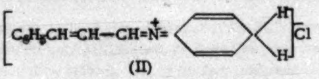
Amine	Acid	M.p.	
		Low-melting form	High-melting form
Aniline.	Hydrochloric	80-82°	151-152°
p-Toluidine. . .		Not formed	168-170°
o-Toluidine . . .		93-95°	Not formed
p-Bromoaniline..	Hydrobromic	101-103	143-144
p-Chloroaniline	Hydrochloric	Not tested	158-159
p-Anisidine . . .		Not formed	158-159
m-Aminophenol		105	Not formed

As with the orthomethylanil, the other low-melting salts are dark-yellow or orange, are readily hydrolyzed into an aldehyde and an amine when boiled, react vigorously with a soda solution, liberating carbon dioxide, and are freely soluble in water. The high-melting isomers, on the other hand, are golden-yellow, remain practically unhydrolyzed when boiled, react less strongly with a soda solution (sometimes the only way to secure the base is to let the salt stand for a long time in a soda solution), and are much less soluble in water.

The behavior and properties of the salts indicate that their formulas are:

$$[C_6H_5CH{=}CH{-}CH{=}\overset{+}{N}HC_6H_5]\overset{-}{Cl}$$

(I)
Low-melting modification



(II)
High-melting modification

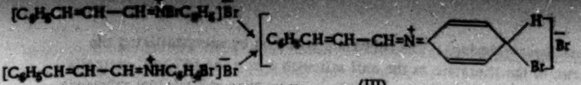
We investigated the bromination of cinnamylideneaniline to secure experimental confirmation of the foregoing structure.

This bromination was first performed by Schiff [2], who secured a yellow powder, which he stated had a m.p. of 175° after recrystallization from alcohol and was a dibromide, according to his analysis. Schiff assigned it the structure of $C_6H_5CHBr{-}CHBr{-}CH{=}N{-}C_6H_5$ for no apparent reason whatsoever.

James and Judd [3] returned to this problem. By reacting bromine with cinnamylideneaniline dissolved in glacial acetic acid they secured an orange-yellow powder with a m.p. of 196-198°, which was decomposed by sodium ethylate into parabromoaniline and cinnamaldehyde. This led the authors to conclude that Schiff's formula was wrong, as the cinnamaldehyde was regenerated, although they themselves proposed to refrain from settling the problem of the structure of the dibromide conclusively, confining themselves to the formula $C_6H_5{-}CH{=}CH{-}CH{=}N{-}C_6H_5{\cdot}Br_2$.

We repeated the bromination of cinnamylideneaniline, again doing so in a glacial acetic acid solution. The very first batches of the halogen produced the strong precipitation of an orange precipitate, which was filtered out after the end of the reaction, washed with glacial acetic acid, and dried in air. The substance fused to a red liquid at 166-167°. Its properties resembled those of the low-melting salts of cinnamylideneaniline, being freely soluble in water, insoluble in ether, evolving carbon dioxide violently when reacted with soda, being partially hydrolyzed when boiled in water, yielding cinnamaldehyde, but undergoing very rapid change when stored. When recrystallized from hot water, it yielded a conversion product, a substance with a m.p. of 143-144°. The hydrobromide of parabromocinnamylideneaniline, prepared from the parabromoanil and hydrobromic acid (m.p. 101-103°) and converted into the high-melting form (m.p. 143-144°) by recrystallization, exhibited no depression of the melting point when mixed with the substance we had synthesized; their properties were wholly alike, and, hence, they were identical.

The fact that the dibromide of cinnamylideneaniline and the hydrobromide of the parabromoanil prepared in the cold were two different substances but both exhibited the properties of salts and both were converted into the same substance when recrystallized is convincing evidence that their structure must be that of (III):



(III)

It is not impossible that the low-melting form of the hydrobromide of the parabromoanil occurs as a transient intermediate product of the conversion of the dibromide. Another variant of the dibromide's structure is theoretically possible: $C_6H_5CH{=}CH{-}CHBr{-}NBr{-}C_6H_5$, but it must be discarded. The saltlike nature of the substance is prime evidence against this structure.

We have found the same state of affairs to prevail when the anil is chlorinated. The hydrochloride of parachlorocinnamylideneaniline with a m.p. of 158-159° (after recrystallization from water) corresponds with the cinnamylideneaniline dichloride synthesized by Staudinger [4] in all its properties. This justifies our adopting the structure of the two forms of the hydrohalides of cinnamylideneaniline set forth above.

EXPERIMENTAL

1. Cinnamylideneaniline. 9.3 g (0.1 mole) of freshly distilled aniline was dissolved in 15 ml of 96% alcohol. 13.2 g (0.1 mole) of cinnamaldehyde diluted with an equal quantity of alcohol, was added to the solution. The mixture was gently heated, turning into a yellow mass within a few minutes. After recrystallization from alcohol the substance fused into a transparent liquid at 106-107°. The yield was 80% of the theoretical.

4.271 mg substance: 0.265 ml N_2 (19°, 751 ml). 3.914 mg substance: 0.216 ml N_2 (19°, 766 mm). Found %: N 7.17, 6.50. $C_{15}H_{13}N$. Calculated %: N 6.76.

Cinnamylideneaniline is an unstable substance, quickly turning red when exposed to air and acquiring an intensive isonitrile odor. For this reason a freshly prepared product was employed in all our subsequent experiments. The anil is decomposed even faster when exposed to sunlight. It does not distil with steam, but is gradually hydrolyzed, so that the distillate always is found to contain aniline and cinnamaldehyde plus (at times) a minute amount of cinnamic acid. Analysis after storage for two years in a colorless bottle gave no indication of a homogeneous substance. Analysis for nitrogen after one month of storage yielded the following results:

3.800 mg substance: 0.286 ml N_2 (17°, 765 mm). 3.743 mg substance: 0.250 ml N_2 (16°, 786 mm). 3.547 mg substance: 0.243 ml N_2 (17°, 744 mm). Found %: N 8.92, 7.86, 7.93. $C_{15}H_{13}N$. Calculated %: N 6.76. In other words, it is the part of the compound that is poorer in nitrogen that decomposes.

An attempt to secure the anil in an alkaline medium was unsuccessful, the greenish product that resulted turning into tar when we tried to recover it in the pure state.

2. The hydrochloride of the anil. The best of all the methods tried out for synthesizing a salt of cinnamylideneaniline consists of triturating the freshly prepared anil with a slight excess of hydrochloric acid (sp.gr. 1.19) at room temperature. This yielded an orange-colored mass, which was washed in as little water as possible and dried between sheets of filter paper and then for a long time in air, after which its m.p. was 80-82°. The salt readily undergoes change in storage, ultimately turning into a substance with a m.p. of 149-151° after standing for 24 hours. This change takes place in the solid phase in a desiccator above H_2SO_4, in the open air, and in a sealed ampoule. It takes place most rapidly when heated in a solvent, especially in water.

Numerous analyses of the substance failed to yield satisfactory results, the percentage of nitrogen fluctuating from 4.5% to 5.5%, as against the 5.71% calculated for $C_{15}H_{13}N \cdot HCl$.

The substance is freely soluble in water, hydrolyzing partially when its aqueous solution is heated and yielding cinnamaldehyde (phenylhydrazone, m.p. 168°) and aniline (bleaching powder reaction), the residue turning into the high-melting product. It reacts like a true salt with carbonates, liberating CO_2 as well as the original anil.

This substance may be secured by directly reacting cinnamaldehyde with aniline in concentrated hydrochloric acid. In one instance it was secured quantitatively by pouring a mixture of 13.2 g of cinnamaldehyde and 10 ml of hydrochloric acid (sp.gr. 1.19) into an equimolecular quantity of aniline.

A saturated NaCl solution throws down the salt from its aqueous solutions.

3. Isomerization product of the anil hydrochloride. The substance produced by recrystallizing the cinnamylideneaniline hydrochloride, known in the literature as the anil salt with a m.p. of 147-148°, actually has a m.p. of 151-152°. Its color is golden-yellow. It is much less soluble in water than the original substance, and it reacts very slowly with a soda solution. Its crystals turn green when exposed to air and exhibit an excessively low value for the percentage of nitrogen.

4.643 mg substance: 0.204 ml N_2 (14°, 757 mm). Found %: N 5.21. $C_{15}H_{13}N \cdot HCl$. Calc.%: N 5.75.

When this salt is reacted with alkalis or soda, it yields a slightly greenish, almost colorless base with a m.p. of 110°. The base is completely stable in air and has no isonitrile odor. When it is recrystallized from alcohol or merely heated, it is transformed into the usual form of cinnamylideneaniline with a m.p. of 106-107°. In none of its other properties does it differ from cinnamylideneaniline.

Both of these salts are soluble in alcohol and acetone and insoluble in ether. When reduced with tin in a hydrochloric medium, both of them break down into their constituents: aniline and cinnamaldehyde.

4. Paramethylcinnamylideneaniline and orthomethylcinnamylideneaniline and their salts. The paramethylanil was prepared in alcohol by pouring together equimolecular quantities of paratoluidine and cinnamaldehyde; its m.p. was 83° after recrystallization from alcohol. In contrast to the anil proper, it does not acquire the odor of an isonitrile upon standing, although it does undergo a change.

We were able to isolate the salt only in one form. It had a m.p. of 168-170° whether isolated in the cold or after recrystallization from alcohol.

3.814 mg substance: 0.178 ml N_2 (17°, 753 mm). Found %: N 5.44. $C_{16}H_{14}N \cdot HCl$. Calc.%: N 5.44

The base regenerated from the salt had a m.p. of 83-84°, but, as in the case of the anil, its color was not the original yellow, but rather slightly greenish, and underwent no change even when kept for months exposed to air. It may be supposed that the substance is converted into the usual form that is stable in storage, even before it reaches its melting point, as we have seen in recrystallization from alcohol, for example.

The orthomethylanil was prepared similarly; its m.p. was 73°. This substance, on the other hand, yields nothing but the low-melting salt, m.p. 93-95°. It is largely hydrolyzed when recrystallized from water, but again melts at 93-95°.

4.000 mg substance: 0.194 ml N_2 (16°, 762 mm). Found %: N 5.67. $C_{16}H_{15}N \cdot HCl$. Calc.%: N 5.44.

The salts of both of these methylanils are likewise unstable, undergoing change when exposed to air, finally being converted into an amorphous mass.

5. Paramethylcinnamylideneaniline methiodide. 2.21 g (0.01 mole) of paramethylcinnamylideneaniline was dissolved in ether to which a few drops of benzene had been added. Twice the theoretical quantity of methyl iodide was then added to the solution. Fifteen days later the red-brown crystals were filtered out and boiled with ethyl alcohol. The substance fused at 196°, without decomposition, to a black liquid. It is extremely stable, withstanding brief heating over a naked flame, but then decomposing with the evolution of yellow fumes. It is nearly insoluble in alcohol, remaining unchanged in boiling water. It does not react with bicarbonate in the cold or when boiled. Microscopic examination showed cubic prisms.

3.347 mg substance: 0.120 ml N_2 (18°, 745 mm). Found %: N 3.74. $C_{17}H_{18}NI$. Calc.%: N 3.85.

6. Brominating cinnamylideneaniline. 4.14 g (0.02 mole) of the anil was dissolved in 25 ml of glacial acetic acid. A solution of 3.6 g of bromine in glacial acetic acid was gradually added to the cherry-red solution, causing the precipitation of a deposit that resembles the anil salts. The m.p. was 166-167° after washing with acetic acid and drying on the filter. It dissolves in water like a typical anil salt and is hydrolyzed when its solution is heated, liberating cinnamaldehyde. It changes fairly rapidly when exposed to air and yields a base when reacted with bicarbonate.

Like all the anil salts, it does not yield satisfactory results upon analysis, owing to its comparatively rapid decomposition.

4.086 mg substance: 0.108 ml N_2 (16°, 772 mm). Found %: N 3.17. $C_{15}H_{13}NBr_2$. Calc.%: N 3.81.

Two days later analysis yielded different findings:

3.800 mg substance: 0.173 ml N_2 (16°, 779 mm). Found %: N 4.36.

Recrystallizing the salt from water converted it into another form, with a m.p. of 143-144°, which proved to be parabromocinnamylideneaniline hydrobromide.

The latter salt was synthesized by a different method for the sake of comparison.

We first synthesized the parabromoanil from cinnamaldehyde and parabromoaniline (m.p. 120-121°) and then secured the salt itself, with a m.p. of 101-103°, by reacting the product with hydrogen bromide in the cold. This salt is readily transformed into the higher-melting form, its m.p.being 143-144° after recrystallization from hot water.

The appearance and the properties of this salt and of the cinnamylideneaniline dibromide are identical. Their mixed melting point is 143-144°, without depression.

7. The p-chloroanil's hydrochloride. The hydrochloride of the parachloroanil was synthesized analogously. Its m.p. was 158-159° after recrystallization from hot water, which corresponds to the "dichloride" of cinnamylideneaniline (m.p. 158°) described in the literature and prepared by chlorinating the anil directly The salt is likewise unstable in air, gradually undergoing a change, though recrystallization,even from boiling water, yields extremely minute quantities of cinnamaldehyde and the amine, i.e., practically no hydrolysis takes place. All of its properties and its appearance are the same as those of the anil's dichloride.

The action of alkalies and of soda regenerates the initial parachloroanil in a slightly greenish form, which is as stable in air as the corresponding forms of the other anils described above.

SUMMARY

1. A study has been made of the isomerization of salts of cinnamylideneaniline.

2. Formulas are suggested for the structure of the resultant products.

3. A study has been made of the bromination of cinnamylideneaniline and the structure of the resultant substances has been demonstrated.

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Received April 24, 1950

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THE SYNTHESIS OF m-AMINO(HYDROXY)-PHENYL-β-(METHYLAMINO)-ETHANOLS AND THE CATALYTIC REDUCTION OF m-NITROACETOPHENONE

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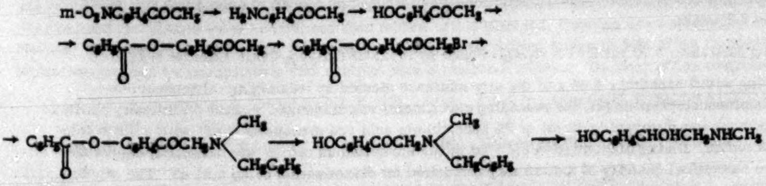
In order to synthesize m-aminophenyl-β-(methylamino)-ethanol (m-$NH_2C_6H_4CHOHCH_2NHCH_3$), which has not been described in the literature, we chose a procedure in which we first condensed m-nitro-ω-bromoacetophenone with benzylmethylamine and then reduced the resulting amino ketone. This procedure seemed to us to be convenient because of the availability of the initial substances: m-nitroacetophenone and m-nitro-ω-bromacetophenone. Our experiments on the condensation of m-nitro-ω-bromoacetophenone with benzylmethylamine showed that the reaction was concluded within 3 hours, the yield of the refined amino ketone hydrochloride reaching 68-70% of the theoretical.

The next stage, the catalytic hydrogenation of m-nitro-ω-(methylbenzylamino)-acetophenone, is more complicated than the hydrogenation of the analogous aryl (methylbenzylaminoalkyl) ketones that are not ring-substituted or whose rings contain hydroxyl groups, since in this case the molecule contains the readily reduced nitro group, in addition to the benzyl and carbonyl group. In the hydrogenation of m-nitro-(methylbenzylamino)-acetophenone with palladium black at atmospheric pressure and at 20-25° all the 5 moles of hydrogen required for the formation of m-aminophenyl-β-(methylamino)-ethanol were absorbed, though the reaction was clearly of a step-by-step nature: the first three moles of hydrogen were absorbed very quickly, after which the reaction slowed down somewhat, the last mole of hydrogen being absorbed extremely slowly. The quantity of hydrogen absorbed quickly (3 moles) seemed to show that the nitro group was first reduced, though the literature suggested [1] that this was followed by the reduction of the benzyl group, with the carbonyl group the last to react.

To test this hypothetical reaction sequence we ran experiments in which hydrogenation was broken off after only 3 moles of hydrogen had been absorbed and after 4 moles had been absorbed. The first reaction yielded m-amino-ω-(methylbenzylamino)-acetophenone dihydrochloride, the second yielding m-amino-ω-(methylamino)-acetophenone dihydrochloride; these findings corroborated our reasoning.

When m-nitro-ω-(methylbenzylamino)-acetophenone was hydrogenated (again at atmospheric pressure) with a Raney nickel catalyst, only the nitro group was reduced, the resultant m-amino-ω-(methylbenzylamino)-acetophenone hydrochloride being recovered as its acetyl derivative. As for the m-aminophenyl-β-(methylamino)-ethanol, it was rather difficult to secure its dihydrochloride in crystalline form, which is in conformity with the data in the literature on similar compounds. The substance was purified by repeated reprecipitation of its ester from alcoholic solutions, a colorless powder being formed after prolonged standing in a vacuum desiccator above P_2O_5; we were unable to determine the melting point of this powder owing to its extremely high hygroscopicity. The structure of m-aminophenyl-β-(methylamino)-ethanol was proved by diazotizing it and converting the diazo compound into an azo dye by coupling it with β-naphthol and by decomposing it with water into racemic m-hydroxyphenyl-β-methylaminoethanol (hydrochloride). Though the latter has been described in the literature, it was synthesized as follows for the sake of a complete comparison:



$$\text{m-}O_2NC_6H_4COCH_3 \rightarrow H_2NC_6H_4COCH_3 \rightarrow HOC_6H_4COCH_3 \rightarrow$$

$$\rightarrow C_6H_5\underset{\underset{O}{\|}}{C}—O—C_6H_4COCH_3 \rightarrow C_6H_5\underset{\underset{O}{\|}}{C}—OC_6H_4COCH_2Br \rightarrow$$

$$\rightarrow C_6H_5\underset{\underset{O}{\|}}{C}—O—C_6H_4COCH_2N\begin{cases}CH_3\\CH_2C_6H_5\end{cases} \longrightarrow HOC_6H_4COCH_2N\begin{cases}CH_3\\CH_2C_6H_5\end{cases} \longrightarrow HOC_6H_4CHOHCH_2NHCH_3$$

In carrying out these reactions, the new factor was the catalytic reduction of m-nitroacetophenone. The catalyst used was either palladium on charcoal or Raney nickel. The nickel catalyst is particularly useful for reactions involving large quantities. The method of catalytic reduction of m-nitroacetophenone possesses many advantages over the noncatalytic methods cited in the literature [2]. The m-aminoacetophenone produced by this method has a m.p. of 95-98° and is fully satisfactory for synthetic purposes; its yield was 95% of the theoretical.

Nor does the literature contain any description of the methods of synthesizing and the properties of some intermediate compounds of the foregoing set of reactions [m-benzoyl-hydroxyacetophenone, m-benzoylhydroxy-ω-bromoacetophenone, and m-benzoylhydroxy-ω-(methylbenzylamino)-acetophenone], so that we have cited them in the experimental section of this paper.

The m-hydroxyphenyl-β-(methylamino)-ethanol hydrochloride synthesized by the above method proved to be identical with the compound synthesized from m-aminophenyl-β-(methylamino)-ethanol by diazotizing it and decomposing the diazo compound.

EXPERIMENTAL

The initial substance, m-nitrobromoacetophenone, was prepared by brominating m-nitroacetophenone dissolved in chloroform [3]. The m-nitro-ω-benzylmethylaminoacetophenone hydrochloride was prepared as follows: 4 g of m-nitro-ω-bromoacetophenone and 24 ml of absolute benzene were placed in a three-necked flask fitted with a stirrer and a calcium chloride tube and chilled to 3-5°, after which 3.96 g of benzylmethylamine was added a drop at a time to the chilled mixture. The mixture was stirred for 4 hours, and then the precipitated benzylmethylamine hydrochloride was filtered out. The yield was 3.08 g; the yield should have been 3.28 g theoretically. The benzene was driven off from the filtrate in vacuo on a water bath at a bath temperature of 30-40°, the remaining reddish hyaline substance being dissolved in absolute ether. The ether solution was filtered, and an ether solution of hydrogen chloride was added to it from a buret, which caused a light-yellow, readily deliquescent precipitate to settle out. The substance had a m.p. of 171-177° with decomposition after filtration and washing with acetone. The yield was 3.6 g or a 68.7 % yield. After recrystallization from a mixture of absolute ethyl alcohol and methanol (3:1), m-nitro-ω-benzylmethylaminoacetophenone hydrochloride fused at 178° with decomposition.

4.932 mg substance: 0.403 ml N_2 (26.5°, 729 mm). 5.076 mg substance: 0.400 ml N_2 (23.5°, 729.7 mm). Found %: N 8.93, 8.71. $C_{16}H_{16}O_3N_2 \cdot HCl$. Calculated %: N 8.73.

m-Aminophenyl-β-methylaminoethanol dihydrochloride. 1.2 g of $PdCl_2 \cdot 2H_2O$ was dissolved in 10 ml of distilled water containing 5-6 drops of concentrated hydrochloric acid, 20 ml of ethyl alcohol was added, and the whole was agitated in an atmosphere of hydrogen. 2 grams of m-nitro-ω-benzylmethylaminoacetophenone hydrochloride, dissolved in 20 ml of ethyl alcohol, was added to freshly reduced palladium black, and the whole was agitated in an atmosphere of hydrogen at 23-25°. 700 ml of hydrogen, or the quantity theoretically required, was absorbed during 1 hour 33 min. After the absorption of hydrogen stopped, the catalyst was filtered out and the solvent driven off in vacuo, leaving behind a slightly yellowish oil, which was dried in a vacuum desiccator above P_2O_5 for 8-10 hours to eliminate any vestiges of moisture. Adding ether to an alcoholic solution of the substance threw down a colorless amorphous precipitate, which was so hygroscopic as to render determination of its melting point impossible. The synthesized amino alcohol was reprecipitated several times from an alcoholic solution by ether and dried in a vacuum desiccator above P_2O_5, after which it was found to be a colorless powder that rapidly deliquesced and reddened when exposed to the air. The yield was 0.81 g, or 54%.

The m-aminophenylmethylaminoethanol dihydrochloride is freely soluble in water (without being hydrolyzed) and in absolute alcohol, its alcoholic solution exhibiting no change in color when it is stored in the dark for 2-3 weeks.

4.862 g substance: 3.93 ml 0.01 N H_2SO_4. Found %: N 11.32; $C_9H_9ON_2 \cdot 2HCl$. Calc.%: N 11.70.

Coupling with β-naphthol. 0.63 g of the oily substance secured by reducing m-nitrophenyl-ω-benzylmethylaminoacetophenone (cf. the preceding experiment) was diazotized without preliminary purification. The substance was dissolved in 12 ml of 7% hydrochloric acid and diazotized at −3° with a 0.5 N solution of sodium nitrite. During diazotization 5.47 ml of the 0.5 N sodium nitrite was absorbed, equivalent to 0.188 g (the theoretical quantity of sodium nitrite required for diazotization being 0.21 g). The solution of the diazo compound was partially neutralized with soda and slowly poured into a chilled solution containing 0.35 g of β-naphthol[*]; a bright-red amorphous precipitate was thrown down; it was filtered out 3-4 hours later, washed with small amounts of cold water, and dried in a vacuum desiccator. The dry dye was triturated a few times in a mortar with ether to eliminate organic impurities, filtered, and dried.

4.906 mg substance: 0.513 ml N_2 (21°, 728 mm). 3.305 mg substance: 0.344 ml N_2 (22.5°, 735.5 mm). Found %: N 11.63, 11.64. $C_{19}H_{19}O_2N_3 \cdot HCl$. Calculated %: N 11.74.

Conversion of m-aminophenyl-β-(methylamino)-ethanol into m-hydroxyphenyl-β-(methylamino)-ethanol. 0.3 g of m-aminophenyl-β-methylaminoethanol hydrochloride (unrefined) was dissolved in 25 ml of 10% hydrochloric acid; the solution was chilled to 3° and diazotized with an 0.5 N solution of sodium nitrite while stirred (until iodized starch paper turned blue). Stirring was continued for another 10-15 minutes to complete diazotization, after which the solution was slowly heated to 80° on a water bath and kept at that temperature until no more nitrogen was evolved. The solution acquired a slightly pinkish color. The water was driven off in vacuo to dryness, absolute ethyl alcohol being added to the residue and the residue of insoluble sodium chloride filtered out. The alcohol was driven out of the filtrate in vacuo, and the residual mass was dried in a vacuum desiccator above P_2O_5. The resultant dark-brown, oily substance was dissolved in a small quantity of absolute ethyl alcohol, and absolute ether was added until the solution turned cloudy. After some time had elapsed, an oil separated from the solution; the solution was decanted from the oil into a clean flask, and ether was again added to this solution until it turned cloudy; some 40-50 minutes later pale-yellow crystals began to settle out. This yielded 0.09 g of a substance that had a m.p. of 131-136° (with decomposition). When absolute ether was added to the mother liquor, another 0.04 g of a more faintly colored substance with a m.p. of 136-139° (with decomposition) settled out.

The two substances were combined, and were purified by repeated reprecipitation from an alcoholic solution with ether, yielding a colorless crystalline substance with a m.p. of 139-141°. The mixed melting point of the substance thus synthesized with the m-hydroxyphenylmethylaminoethanol prepared by reducing m-hydroxy-ω-benzylmethylaminoacetophenone exhibited no depression.

8.035 mg substance: 3.74 ml 0.1 N H_2SO_4. Found %: N 6.52. $C_9H_{13}O_2N \cdot HCl$. Calculated %: N 6.87.

m-Amino-ω-benzylmethylaminoacetophenone dihydrochloride. 1 g of m-nitro-ω-benzylmethylaminoacetophenone was dissolved in 40 ml of methanol and agitated in hydrogen with palladium black, prepared by reducing 1 g of palladium chloride. Hydrogenation was broken off after 200 ml of hydrogen had been absorbed within 10 minutes, after which the reaction slowed down greatly (210 ml of hydrogen being required theoretically to reduce the nitro group). The catalyst was filtered out, the solvent was driven off in vacuo, and the residue was dried in a vacuum desiccator above P_2O_5. We were unable to crystallize the resultant light-brown hyaline mass The substance was purified by converting it into a base by adding an aqueous solution of ammonia until its reaction was strongly alkaline. The base was extracted with ether, the ether solution was dried with potash, and then an ether solution of hydrogen chloride was added from a buret a drop at a time until the reaction to Congo red was acid. The dihydrochloride settled out as a colorless flocculent precipitate that quickly deliquesced in air. The precipitate was washed a few times with absolute ether and dried in a vacuum desiccator over P_2O_5 The product was a colorless, extremely hygroscopic powder Its high hygroscopicity made it impossible to determine its melting point.

6.696 mg substance: 4.12 ml 0.1 N H_2SO_4. 8.087 mg substance: 4.79 ml 0.1 N H_2SO_4. Found %: N 8.61, 8.29. $C_{16}H_{18}ON_2 \cdot 2HCl$. Calculated %: N 8.56.

m-Amino-ω-methylaminoacetophenone dihydrochloride. A solution of 2 g of m-nitro-ω-benzylmethylaminoacetophenone hydrochloride in 60 ml of ethyl alcohol was added to freshly reduced palladium black, prepared from 1.2 g of $PdCl_2 \cdot 2H_2O$, and the mixture was agitated in hydrogen until 500 ml of hydrogen was absorbed (the amount theoretically required to reduce the nitro group and split off the benzyl group), and then the reaction was broken off. The catalyst was filtered out, and the filtrate was evaporated in vacuo to dryness. The oily residue was dissolved in absolute ethyl alcohol and then rubbed with a glass rod, throwing down a colorless amorphous precipitate, which was filtered out and washed with alcohol. This yielded 0.55 g or 37% of the theoretical. The substance was purified by precipitation with acetone from a methanol solution. Decomposition temperature: 208°.

4.110 mg substance: 0.446 ml N_2 (28.5°, 731.3 mm). 5.902 mg substance: 7.024 mg AgCl. 5.868 mg substance: 6.985 mg AgCl.
Found %: N 11.79; Cl 29.44, 29.45. $C_9H_{12}ON_2 \cdot 2HCl$. Calculated %: N 11.81. Cl 29.94.

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[*]) The coupling solution of β-naphthol was prepared by the method given by Fierz-David: 0.1 mole of β-naphthol, 15 ml of a 30% solution of NaOH, and 25 g of soda were dissolved in the necessary quantity of water.

m-Acetylamino-ω-benzylmethylaminoacetophenone hydrochloride. 0.5 g of m-nitro-ω-benzylmethylaminoacetophenone was dissolved in 20 ml of methanol, and the solution was agitated with 0.5 g of a Raney nickel catalyst in an atmosphere of hydrogen. 110 ml of hydrogen was absorbed in 6 hours at 16-18° (theoretically 105 ml of hydrogen was required to neutralize the nitro group), after which further absorption of hydrogen ceased. The substance secured after the catalyst had been filtered out and the solvent driven off in vacuo did not crystallize; it was heated on a water bath for 10-15 minutes with an excess of acetic anhydride, after which a small portion of the oily product was transferred to a watch glass and triturated with acetone, yielding crystals that were utilized as seeds. The crystallized mass was washed with acetone, yielding 0.3 g of a colorless substance that fused at 193-195° with decomposition. The m.p. of the substance was 206-207° after recrystallization from absolute ethyl alcohol; it was freely soluble in aqueous ethyl alcohol, but insoluble in acetone, ethyl acetate, or petroleum ether.

6.283 mg substance: 3.64 ml 0.01 N H_2SO_4. 3.345 mg substance: 1.94 ml 0.01 N H_2SO_4.
Found %: N 8.11, 8.12. $C_{18}H_{20}O_2N_2 \cdot HCl$. Calculated %: N 8.40.

Catalytic Reduction of m-Nitroacetophenone

a) Reducing m-nitroacetophenone with 10% palladium on charcoal. 1 g of m-nitroacetophenone was dissolved in 25 ml of ethyl acetate and then agitated in hydrogen with 0.1 g of the catalyst at room temperature (18-20°) and atmospheric pressure. During the course of 20 minutes 410 ml of hydrogen was absorbed (406 ml being called for theoretically). The catalyst was filtered out, and the solution was evaporated in vacuo, yielding m-aminoacetophenone as a crystalline precipitate with a m.p. of 89-91°. Recrystallization from water yielded 0.58 g of m-aminoacetophenone with a m.p. of 94.5-96°. The yield was 71%.

b) Reduction with Raney nickel. We ran numerous experiments in the course of our study of the optimum conditions for reducing m-nitroacetophenone with Raney nickel. The best conditions are described below. 20 g of m-nitroacetophenone was dissolved in 150 ml of ethyl acetate and then agitated with 10 g of the catalyst in hydrogen at 20-25°. The theoretical quantity of hydrogen (8140 ml) was absorbed within 90-120 minutes. After the catalyst had been filtered out and the solvent driven off in vacuo there was left behind in the flask an oily substance that quickly crystallized; m.p. 94-96°. This yielded 15.5 g of m-aminoacetophenone (94.7%).

Synthesis of m-hydroxyphenyl-β-(methylamino)-ethanol. m-Benzoylhydroxyacetophenone was prepared by reacting 5.5 g of m-hydroxyacetophenone* dissolved in 25 ml of pyridine with 1.5 g of benzoyl chloride. Recrystallization from petroleum ether yielded 8.4 g (86.6%) of colorless acicular crystals with a m.p. of 47-51°. The m.p. was raised to 52-53° after another recrystallization from aqueous alcohol.

3.069 mg substance: 8.478 mg CO_2; 1.399 mg H_2O.
Found %: C 75.34; H 5.10. $C_{15}H_{12}O_3$. Calculated %: C 74.99; H 5.03.

m-Benzoylhydroxy-ω-bromoacetophenone.** We used 10 g of m-benzoylhydroxyacetophenone in 50 ml of chloroform and 7 g of bromine in 10 ml of chloroform. After the reaction was over and the solvent had been driven off, the residue was washed with small portions of ether and then recrystallized from alcohol. This yielded 10.8 g of a substance with a m.p. of 99-102°. The substance was fully stable toward ethyl alcohol, freely soluble in acetone and chloroform, and sparingly soluble in petroleum ether and benzene. A sample prepared for analysis had a m.p. of 105-106°.

0.2072 g substance: 0.1212 g AgBr. 0.2046 g substance: 0.1198 g AgBr.
Found %: Br 24.89, 24.96. $C_{15}H_{11}O_3Br$. Calculated %: Br 25.05.

m-Benzoylhydroxy-ω-benzylmethylaminoacetophenone hydrochloride. 4 g of m-benzoylhydroxy-ω-bromoacetophenone and 20 ml of absolute benzene were placed in a three-necked flask fitted with a stirrer and a calcium chloride tube, and 3.03 g of benzylmethylamine was added drop by drop to the suspension, which was thoroughly stirred and chilled externally with ice.

Stirring was continued for 3-4 hours, after which the precipitated benzylmethylamine hydrobromide was filtered out. The yield was 2.28 g, theory calling for 2.4 g. The filtrate was evaporated in vacuo to dryness, the residue being dissolved in absolute ether. The ether solution turned slightly cloudy; it was filtered through a pleated filter, and the chilled filtrate was stirred while an ether solution of hydrogen chloride was added from a buret until the reaction to Congo red was acid. The light-yellow amorphous precipitate of m-benzoylhydroxy-ω-benzylmethylaminoacetophenone that was thrown down was highly hygroscopic. The precipitate was transferred as quickly as possible to a filter together with the ether and washed several times with absolute ether, always leaving some ether in the funnel. The precipitate, moistened with ether, was dried in a vacuum desiccator. The yield was 3.88 g (78.3%). The substance was freely soluble in absolute ethyl alcohol, methanol, and acetone, and insoluble in ether. Its aqueous solution hydrolyzed readily. The unpurified m-benzoylhydroxy-ω-benzylmethylaminoacetophenone hydrochloride was then analyzed.

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* m-Hydroxyacetophenone was prepared from m-aminoacetophenone by the Rupe and Majewski method [4].

** m-Benzoylhydroxy-ω-chloroacetophenone is employed as the initial substance in the patents.

0.0403 g substance: 7.3 ml 0.015 N HCl. Found %: N 3.80. $C_{23}H_{22}O_3N \cdot HCl$. Calc.%: N 3.54.

m-Hydroxy-ω-benzylmethylaminoacetophenone hydrochloride. 4 g of m-benzoyl-hydroxy-ω-benzylmethylaminoacetophenone hydrochloride was refluxed on a water bath in a round-bottomed flask for 6 hours with 10 ml of a 10% alcoholic solution of hydrogen chloride. Driving off the solvent in vacuo left behind a dark, oily substance, which crystallized when chilled or when a small quantity of acetone was added. After recrystallization from absolute ethyl alcohol the m-hydroxy-ω-benzylmethylaminoacetophenone hydrochloride was a colorless crystalline substance with a m.p. of 200-201° (with decomposition). The yield was 2.2 g (75%). The substance was soluble in methanol, less so in ethyl alcohol; freely soluble in water, and insoluble in acetone; its aqueous solution was not hydrolyzed.

8.098 mg substance: 0.353 ml N_2 (21.5°, 737 mm). 7.578 mg substance: 0.322 ml N_2 (22.5°, 739.5 mm). 5.545 mg substance: 2.675 mg AgCl. 5.810 mg substance: 2.855 mg AgCl. Found %: N 4.90, 4.78; Cl 11.93, 12.20. $C_{16}H_{17}O_2N \cdot HCl$. Calculated %: N 4.80; Cl 12.18.

m-Hydroxyphenylmethylaminoethanol hydrochloride. 1.15 g of m-hydroxybenzylmethyl-aminoacetophenone hydrochloride was dissolved in 50 ml of ethyl alcohol, added to freshly reduced palladium black (prepared from 1 g of $PdCl_2 \cdot 2H_2O$), and agitated in hydrogen at 30°, 180 ml of hydrogen being absorbed within 20 minutes. After the catalyst had been filtered out and the solvent had been driven off in vacuo, the resultant oily substance was dried for 4-5 hours in a vacuum desiccator above P_2O_5. Subsequent trituration with 3 ml of absolute ethyl alcohol yielded a colorless crystalline precipitate. The yield was 0.45 g with a m.p. of 140-141°. The addition of absolute ether to the mother liquor yielded another 0.28 g with a m.p. of 138-141°. Recrystallization of the combined precipitates from alcohol yielded 0.67 g (84%) with a m.p. of 141-142°.

6.731 mg substance: 3.30 ml 0.01 N H_2SO_4. 6.758 mg substance: 3.34 ml 0.01 N H_2SO_4. Found %: N 6.86, 6.92. $C_9H_{13}O_2N \cdot HCl$. Calculated %: N 6.87.

SUMMARY

1. m-Aminophenyl-β-(methylamino)-ethanol has been synthesized; the structure of this compound was proved by converting it into the hydrochloride of the known m-hydroxyphenyl-β-(methylamino)-ethanol.

2. m-Hydroxyphenyl-β-(methylamino)-ethanol has been synthesized by the method proposed.

3. A method is given for synthesizing m-aminoacetophenone catalytically.

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Received March 13, 1950

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THE MECHANISM OF THE WOHL REACTION FOR SYNTHESIZING PHENAZINE

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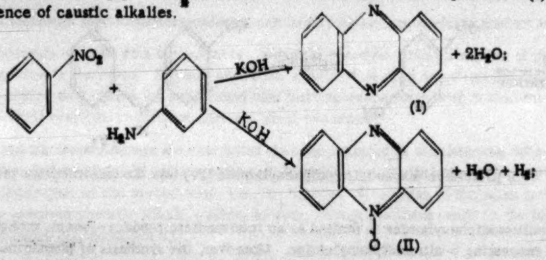
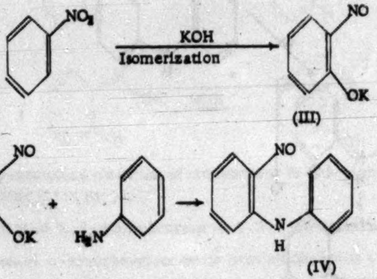
The occasion for our consideration of the Wohl reaction has been an interest in phenazine and some of its derivatives as raw material for the synthesis of microorganism pigments: pyocyanin [1], iodinin [2], and chlororaphin [3].

In the Wohl reaction [4] nitrobenzene* and aniline are condensed to phenazine (I) or phenazine oxide (II) in the presence of caustic alkalies.



Wohl assumed that nitrobenzene was isomerized in the presence of a caustic alkali into the unstable o-nitrosophenol (III) which has not been isolated up to the present time (cf. Diagram I), the o-nitrosophenol reacting with aniline to yield o-nitrosodiphenylamine (IV), which is converted into phenazine oxide (II) when the reaction is carried out at 120-125° and into phenazine (I) at a higher temperature (140-160°). The yield of (I) + (II) was about 15% .

Diagram I



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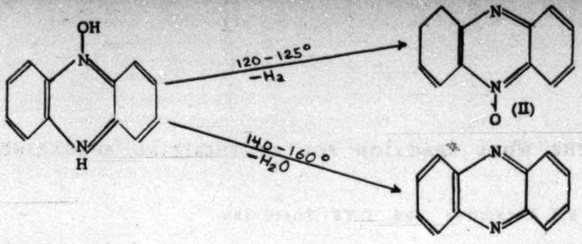
* Analogously, derivatives of nitrobenzene and aniline yield substitution derivatives of phenazine.

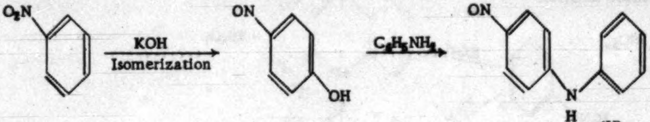


(II)

(1)

Wohl cited the following findings in support of this reaction sequence.

When he treated a water-alcohol solution of the tarry precipitate secured in the reaction with carbon dioxide, he succeeded in isolating p-nitrosophenylamine (V) as a by-product alongside the phenazine. Wohl considered the formation of this compound to result from the reaction of the p-nitrosophenol with aniline [5]:

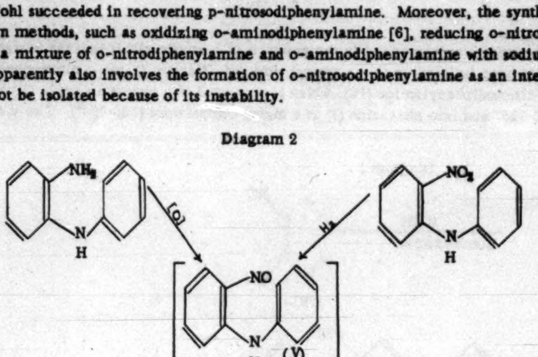


(V)

It was this fact that led Wohl to believe that o-nitrosodiphenylamine (IV) was the intermediate product in the synthesis of phenazine.

This supposition—that o-nitrosodiphenylamine is formed as an intermediate product—seems probable, inasmuch as Wohl succeeded in recovering p-nitrosodiphenylamine. Moreover, the synthesis of phenazine by the other known methods, such as oxidizing o-aminodiphenylamine [6], reducing o-nitrodiphenylamine [7], or, finally, fusing a mixture of o-nitrodiphenylamine and o-aminodiphenylamine with sodium acetate [8] (cf. Diagram 2), apparently also involves the formation of o-nitrosodiphenylamine as an intermediate product, though it cannot be isolated because of its instability.

Diagram 2



In assuming that o-nitrosodiphenylamine is formed as an intermediate product, however, Wohl presupposed that the formation of this compound was an indispensable prerequisite for the isomerization of nitrobenzene to o-nitrosophenol (cf. Diagram 1). Wohl regarded the fact that the action of potassium hydroxide on nitrobenzene at 60-70° produces a 33% yield of potassium o-nitrophenolate plus a small amount of potassium p-nitrophenolate as a proof of such isomerization. (He believed that the nitro compounds were secured by oxidation of the nitroso compounds formed in the initial reaction stage by the excess nitrobenzene).

This supposition cannot be regarded as correct today, for we have learned that the reaction in which nitrophenols are formed from nitrobenzene by fusion with an alkali must be considered a direct hydroxylation of the nitrobenzene, in which there is an "illegal" orientation to the ortho position (see below for substitution reactions of the second kind [5].) In the light of this, Wohl's whole reaction sequence falls to the ground.

To discover the actual course of the reaction, we felt it was first necessary to make an experimental check of whether potassium o-nitrosophenolate can take part in the Wohl reaction.

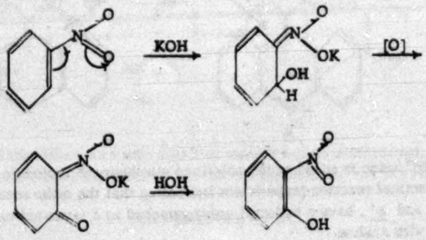
Orthonitrosophenol is a highly unstable product, existing only in solution. We have shown that o-nitrosophenol in solution, prepared as specified by Baudisch [9], exhibits no tendency to enter into a condensation reaction with aniline, whereas the stable naphthalene analog of o-nitrosophenol, 1-nitroso-2-naphthol, does not yield even a trace of benzophenazine when reacted with aniline under the conditions specified by Wohl (140-160°, KOH). If we assume that 1-nitroso-2-naphthol exists primarily as the monooxime of orthoquinone, then condensation with aniline ought to be all the smoother. Moreover, we have shown that phenazine can be synthesized from nitrobenzene and aniline without employing a caustic alkali, provided sodium anilide is used in the reaction instead of aniline and the caustic alkali and the reaction is carried out in xylene.

All this indicates that orthonitrosophenol can hardly be an intermediate product in the Wohl reaction.

Azobenzene is secured as a by-product in the Wohl reaction. The formation of this compound cannot be explained by Wohl's reactions. Nor can azobenzene be looked upon as an intermediate product capable of closing the phenazine ring, since we have found that heating azobenzene with potassium hydroxide and nitrobenzene in the Wohl reaction conditions does not yield phenazine.

Analyzing all these findings we concluded that the reaction of nitrobenzene with aniline in the presence of caustic alkalies (A. Wohl) or of sodium amide (Z.V.Pushkareva, Agibalova [10]) must be regarded as a typical instance of a substitution of the second kind, i.e., an inverted orientation of the nitro group when acted upon by nucleophilic reagents (caustic alkali, sodium amide). These reactions result in the formation of phenazine or of phenazine oxide (cf. Diagram 3).

In these reactions the $(OH)^-$ and $(NH_2)^-$ anions attack those carbon atoms in which the electron density is a minimum owing to the polarization of the nitrobenzene molecule, i.e., in the ortho or para positions. The following reactions are instances of this sort:



1) The above-mentioned oxidation of nitrobenzene to orthonitrophenol when nitrobenzene is fused with solid potassium hydroxide [5] in the air:

2) The amination of 1,3-dinitrobenzene to 1,3,4-dinitroaniline [11].

3) The synthesis of p-nitrophenylcarbazole from nitrobenzene and carbazolesodium [2].

4) The reaction of nitrobenzene with piperidinesodium, yielding p-nitro-N-phenylpiperidine [3].

The amination and hydroxylation of pyridine and quinoline at the α- and γ-positions to the heterocyclic nitrogen [14] instead of the usual substitution at the β- position are other instances of this type of reaction.*

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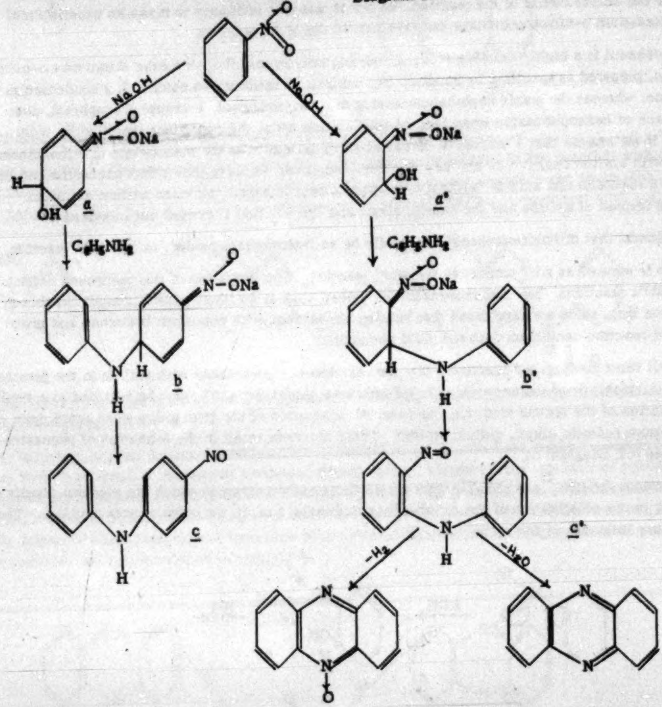
* The nitrogen in the pyridine and quinoline rings plays the same part in orientation as the nitro group in nitrobenzene.

Other examples might be cited of "illegal" orientation, such as the hydroxylation of resorcinol by an alkali [15], the hydroxylation of 1- or 2-hydroxyanthraquinone [16], the hydroxylation of β-anthraquinonesulfonic acid to alizarin when fused together with an alkali, and the condensation of benzenanthrone in fusion with an alkali [17].

In the light of the foregoing, the condensation of nitrobenzene with aniline in the presence of a caustic alkali must be looked upon as follows (cf. Diagrams 3 and 4).

Diagram 3



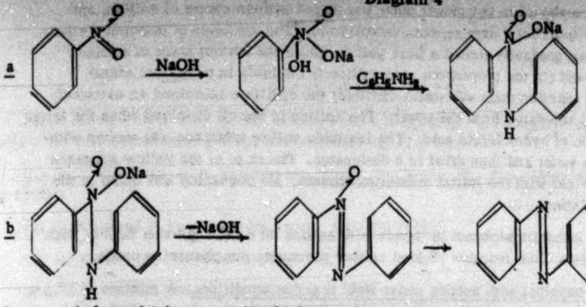
In Diagram 3 the $(OH)^-$ anion is added to the polarized nitrobenzene molecule at the para and ortho positions at the instant of chemical reaction (experiment indicating that the ortho reaction predominates). The resultant compounds, a and a', have a hydroxyl group attached to a saturated carbon atom and are quinols, which react readily with aniline.

The quinanilides b and b' are converted into stable benzene compounds by the splitting off of a molecule of sodium hydroxide (c and c'). As for the side reaction in which azobenzene is formed, this may be represented as involving the addition of a molecule of sodium hydroxide at the nitro group, with the resultant addition product reacting with aniline (cf. Diagram 4, a and b).

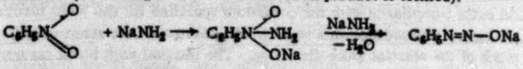
First azoxybenzene is formed, turning into azobenzene under the reaction conditions. (In a special test we have shown that azoxybenzene is converted into azobenzene at 140° when aniline and a caustic alkali are present, i.e., under the conditions of the Wohl reaction).

The addition of sodium amide to the nitrogroup of nitrobenzene has been described already in the literature [18]. When sodium amide is reacted with nitrobenzene for a long time in the cold, sodium

Diagram 4



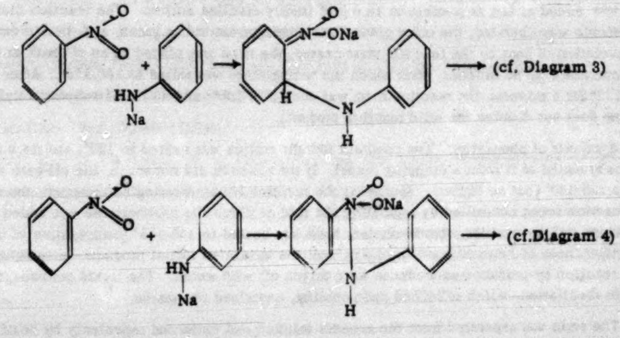
diazotate is formed (via a stage in which an addition product is formed):



$$C_6H_5NO_2 + NaNH_2 \longrightarrow C_6H_5N(O)(ONa){-}NH_2 \xrightarrow[-H_2O]{NaNH_2} C_6H_5N{=}N{-}ONa$$

A particularly striking example of a reaction involving inverted orientation is the formation of phenazine when nitrobenzene is reacted with sodium anilide. By so doing we have managed to secure 30-35% yields of phenazine, based on the reacted nitrobenzene. This reaction may be represented as follows:

Diagram 5



It is not impossible that when a caustic alkali or sodium amide is employed, the Wohl reaction takes place only after sodium anilide has been formed, the latter then entering into the reaction as shown in Diagram 5.

EXPERIMENTAL

Reaction of orthonitrosophenol with aniline. The orthonitrosophenol solution was prepared as specified by Baudisch [9]. 0.5 g of orthonitrophenol was heated in a small quantity of glacial acetic acid until it dissolved, the acetic acid solution being chilled and 1-2 ml of water being added, causing the orthonitrophenol to settle out in a finely crystalline state. Petroleum ether was added to the suspension of orthonitrophenol in acetic acid, and 0.3 g of zinc dust was added to the vigorously shaken mixture. The acetic acid solution turned red, the petroleum ether turning yellow at first, and then green, due to the resultant orthonitrosophenol.[*]

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[*] The formation of the copper salt of orthnonitrosophenol was evidence of the formation of the latter compound. When a petroleum ether solution of orthonitrosophenol was agitated with a highly diluted solution of copper sulfate, the latter turned an intense red, due to the formation of a copper salt of orthonitrosophenol.

The solution of orthonitrosophenol in petroleum ether was mixed with an excess of aniline, and the reaction mass was allowed to stand for 3 days at room temperature. The top layer of petroleum ether, which was an intense green at first, gradually turned a faint yellow, while the bottom layer of aniline changed from yellow to a cherry-red (in the proportions used aniline is insoluble in petroleum ether). After standing for three days, the reaction mass was steam-distilled; the distillate contained an extremely minute quantity of oil, which was separated from the water. The aniline in the oil dissolved when the latter was agitated with a dilute solution of hydrochloric acid. The insoluble yellow substance was washed with dilute hydrochloric acid and with water and then dried in a desiccator. The m.p. of the yellow substance was 43°. The substance was identical with the initial orthonitrosophenol. No phenazine was found in the residue left after the steam distillation.

Heating a solution of the orthonitrosophenol in ligroin with aniline on a boiling water bath or with aniline and potassium hydroxide in a Wohl reaction yielded neither phenazine nor phenazine oxide.

Reaction of 1-nitroso-2-naphthol with aniline under Wohl reaction conditions. A mixture of 17.3 g of 1-nitroso-2-naphthol, 9.3 g of aniline, and 40 g of finely pulverized anhydrous potassium hydroxide was heated to 140-160° for 16 hours, in strict compliance with the conditions specified for the Wohl reaction. Steam was passed through the dark tarry mass produced as a result of the reaction. The steam-distillation residue was washed with water, much of the reaction mass dissolving. The residual dark black tar was extracted with 20% hydrochloric acid. No benzophenazine could be recovered from the hydrochloric acid solution by adding ammonia to it, which is evidence that orthonitrosonaphthol does not react with aniline under Wohl reaction conditions to yield benzophenazine.

Synthesis of Phenazine by Reacting Nitrobenzene with Sodium Amide.

Synthesis of sodium anilide by the Chichibabin method [17]. 7.8 grams of finely pulverized sodium amide was added as fast as possible to 18.6 g of freshly distilled aniline. The reaction mass grew very hot, and ammonia was liberated, the color gradually changing from red to green, and then to dark-brown. As soon as the evolution of heat by the reaction mass ceased, the mass was placed in an oil bath at 120° and kept at that temperature for 20 minutes, after which the temperature was raised to 160.170°. After being heated to 160-170° for 5 minutes, the reaction mass was cooled to 100°, and 40 ml of anhydrous xylene was added to it (xylene does not dissolve the solid reaction product).

Synthesis of phenazine. The resultant sodium anilide was heated to 125°, and 24.6 g of nitrobenzene was slowly added to it from a dropping funnel. If the reaction did not set in, the oil-bath temperature was raised to 135-140° (but no higher). As soon as the reaction began, heating was stopped, the subsequent course of the reaction being controlled by regulating the rate at which the nitrobenzene was added. After all the nitrobenzene had been added, the thick, dark mass was heated to 140-145° (temperature of the oil bath) for 10 hours. After these 10 hours of heating, the xylene, the unreacted initial products—nitrobenzene and aniline, and the reaction by-product—azobenzene were driven off with steam. The liquid resinous mass left after the steam distillation, which solidified upon cooling, contained phenazine.

The resin was separated from the aqueous solution and extracted repeatedly by heating it with small portions of 20% hydrochloric acid. 2-3 ml of concentrated nitric acid were added to the dark hydrochloric acid solution, and the whole was brought to a boil. A resin floated to the top; it was filtered out after the solution had cooled.

The transparent orange-red hydrochloric-acid solution was neutralized with ammonia, throwing down a dark-yellow phenazine precipitate. The resultant phenazine was purified by reprecipitating it once or twice with ammonia from a solution in 20% hydrochloric acid. The phenazine yield was 30-32%, based on the reacted nitrobenzene; m.p. 168-169°. Recrystallization from 10 times its weight of alcohol yielded the characteristic shining yellow needles with a m.p. of 170-171°, exhibiting no depression when mixed with phenazine synthesized by a different method.

SUMMARY

1. It has been shown that the synthesis of phenazine in the Wohl reaction from nitrobenzene and aniline with an alkali present is an instance of the inverted orientation of the nitro group when acted upon by nucleophilic reagents (KOH, $NaNH_2$; cf. Diagram 3).

2. In conformity with this reaction pattern, phenazine has been synthesized by condensing nitrobenzene with another nucleophilic reagent—sodium anilide (cf. Diagram 5).

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Received June 15, 1950

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XXXV. THE CONVERSION OF BUTYROLACTONE INTO THIOPHANONE-2, PYRROLIDONE-2, and 1-PHENYLPYRROLIDONE-2

Yu.K. Yuryev, E.G. Vendelshtein, and L.A. Zinovyeva

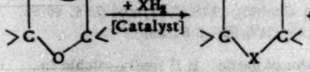
The conditions governing the substitution of an imino group for the bridge oxygen on the lactones of γ- and δ-hydroxy acids vary with the nature of the lactone. The conversion of phenolphthalein into imidophenolphthalein when it is allowed to stand with aqueous ammonia at room temperature [1] and the conversion of phthalide into phthalimidine [2] when ammonia is passed through phthalide at 290° are the extremes in the conditions governing the course of this side reaction.

H. Meyer [3] endeavored to deduce definite rules from the behavior of various γ- and δ-lactones when acted upon by ammonia and concluded that the decisive role is played by the nature of the hydroxyl group in the hydroxy acid yielding the given lactone. This led him to the following conclusions:

1. The reaction of γ- and δ-lactones with ammonia either does not take place at all or results in the formation of a more or less unstable amide of the hydroxy acid when the hydroxyl group is a primary group or a saturated secondary group or is a phenolic one: butyrolactone, γ-valerolactone, and γ-caprolactone could not be converted into the respective lactams, thus supporting the rule, though phthalide was converted into a lactam and, hence, constituted an exception to the rule.

2. γ- and δ-lactones react with ammonia to form imides—lactams of the γ- and δ-amino acids —when the hydroxyl group is a tertiary or a secondary unsaturated one (>C=CHOH): triphenylcrotolactone [4], phthalylacetic acid [5], and phenolphthalein [1] are representatives of compounds of this type.

The catalytic conversions of the original rings of the five-membered and six-membered oxygen-containing heterocyclic compounds into heterocyclic compounds containing nitrogen [6], sulfur [7], and selenium [8] are the natural completion of many years of research on the substitution of an imino group for the ring oxygen in cyclic anhydrides, in γ-pyrone, and in its derivatives. All these reactions must now be regarded as special instances of a reaction involving the replacement of ring oxygen by another hetero atom, which is quite generally applicable to all heterocyclic systems that contain oxygen and takes place under suitable conditions when reagents interact with the active hydrogen atoms:



+ H_2O (X = NH; NAlk; NAr, NPy; S; Se)

Hence, H. Meyer's rule has lost all significance, and, now that furan, the most stable of the oxygen-containing heterocyclic compounds, has been converted into pyrrole by the action of ammonia upon it in the presence of alumina at 450° [6], it is safe to say that the ring oxygen in butyrolactone and γ-valerolactone must be replaced by an imino group under conditions that are milder than those governing the conversion of furan but much more severe than those governing the conversion of other lactones, such as phthalide. The influence of the oxygen atom linked to the α-carbon atom in the ring makes the bond of the ring oxygen in butyrolactone weaker than it is in furan or furanidine, but stronger than in cyclic anhydrides or in substituted lactones, such as triphenylcrotolactone. That is why it is only by heating to 280° with liquid ammonia at considerable pressure that pyrrolidone-2 could be prepared from butyrolactone or 5-methylpyrrolidine-2 from γ-valerolactone [9].*

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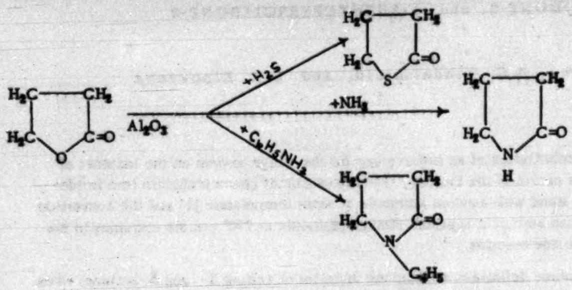
* The authors do not state the pyrrolidone yields.

Butyrolactone must likewise suffer the catalytic substitution of sulfur or of an imino group for its ring oxygen, though at much lower temperatures than in the case of furan and furanidine. Lowering the reaction temperature could not, however, eliminate an appreciable decomposition of butyrolactone, due to its instability.

In the present research butyrolactone has been converted into thiophanone-2 (tetrahydro-α-thienone) by the action of hydrogen sulfide, into pyrrolidone-2 by the action of ammonia, and into 1-phenylpyrrolidone-2 by the action of aniline—all at 350° in the presence of alumina:



EXPERIMENTAL

Conversion of Butyrolactone into Thiophanone-2 (Tetrahydro-α-thienone; Butyrothiolactone)

300°. 8 g of butyrolactone (b.p. 83-85° at 5 mm); n_D^{20} 1.4369; d_4^{20} 1.1288) was passed through a tube containing alumina at the rate of 12 drops per minute in a current of hydrogen sulfide. The catalyzate was extracted with ether. After the ether had been driven off from the ether extract of the catalyzate (which had been dried with calcium chloride), the reaction product was distilled in vacuo, yielding the following fractions: I) b.p. 109.5-110° (51 mm)—2.5 g; and II) b.p. 110-111° (51 mm)—0.3 g. Fraction I was thiophanone-2 (30% of the theoretical yield).

325°. 8 g of butyrolactone yielded 3.5 g of thiophanone-2 (38% of the theoretical yield).

350°. 8 g of butyrolactone yielded 6 g of thiophanone-2 (72% of the theoretical yield).

375°. 8 g of butyrolactone yielded 2.8 g of thiophanone-2 (30% of the theoretical yield).

The thiophanone-2 secured in all the tests was combined and redistilled in vacuo (from a flask with a dephlegmator); its constants then were:

B.p. 110.5 (52 mm); n_D^{20} 1.5189; d_4^{20} 1.1635; MR_D 26.39; calculated 26.45.

Melting point of the compound with corrosive sublimate (from alcohol): 118.5°. Found %: C 46.92, 46.98; H 5.89, 5.86; S 31.24, 31.30. C_4H_6OS. Calculated %: C 47.05; H 5.92; S 31.39.

Thiophanone-2 is a colorless liquid with the characteristic odor of garlic. It is freely soluble in alcohol and in ether, though insoluble in water.

Reduction of thiophanone-2 to thiophane. 5.3 g of thiophanone-2 was reduced by boiling for five hours with 16 g of zinc amalgam and 32 ml of dilute (1:1) hydrochloric acid, with 5 ml of hydrochloric acid (sp.gr. 1.16) added every hour. Then the reaction product was distilled with steam, and the resultant distillate extracted with ether. The ether extract was dried with anhydrous sodium sulfate, the ether driven off, and the residue distilled, yielding 0.8 g of a fraction with a b.p. of 116-122° (757 mm) and n_D^{20} 1.5021, which produced a crystalline compound with $HgCl_2$, whose m.p. was 125° after recrystallization from alcohol. The mixed melting point with a compound of thiophane with mercuric chloride exhibited no depression: m.p. 125°. Hence, the 116-122° fraction was thiophane (tetrahydrothiophene) produced by the reduction of thiophanone-2.

Figures in the literature for thiophane: Yu.K.Yuryev [10]: b.p. 119.8-120° (760 mm); n_D^{20} 1.5052; d_4^{20} 0.9960; m.p. of the compound with mercuric chloride: 124.5-125°.

Conversion of Butyrolactone to Pyrrolidone-2 and 1-Phenylpyrrolidone-2

1) 21 g of butyrolactone was passed over alumina (in 7-gram batches) in a current of ammonia at 350°. The ether extract of the catalyzate was dried with anhydrous sodium sulfate, the ether was driven off, and the residue was distilled in vacuo. Redistillation of the reaction product yielded the following fractions: I) b.p. 95-102°—0.2 g; II) b.p. 102-104° (5 mm)—3.2 g; and III) b.p. 104-110°—0.5 g.

Fraction II was pyrrolidone-2 (15.5% of the theoretical yield).

B.p. 102-104° (5 mm); n_D^{20} 1.4806; d_4^{20} 1.106; b.p. 23-24°. MK_D 21.88; calculated 22.23.
Found %: N 16.56. C_4H_7ON. Calculated %: N 16.44.

Figures in the literature for pyrrolidone-2: Gabriel [11]: b.p. 245°; m.p. 25-28°; Tafel and Stern [12]: b.p. 205.5° (742 mm); m.p. 24.6°; d_4^{20} 1.110 [12]; Späth and Lintner [9]: b.p. 100-105° (1 mm); m.p. 23-24°.

2) A mixture of 7 g of butyrolactone and 20 g of aniline was passed over alumina in a current of nitrogen at 350°. An ether extract of the catalyzate was dried the ether driven off, and the residue distilled in vacuum, repeated redistillation of the reaction product (after the unchanged aniline had been eliminated) yielding the following fractions: I) b.p. 140-150° (5 mm)—3 g; II) b.p. 150-155° (5 mm)—2.1 g; and III) b.p. 155-160° (5 mm)—1.8 g.

Fractions II and III crystallized; crystals settled out of Fraction I upon cooling.

The colorless crystals of 1-phenylpyrrolidone-2 fused at 66-67°. The yield was 4.3 g (32% of the theoretical).

Found %: N 8.78. $C_{10}H_{11}ON$. Calculated %: N 8.69.
Figures in the literature for 1-phenylpyrrolidone-2: Baille and Tafel [14]: m.p. 64-68°; b.p. 130-140° (1 mm); Späth and Lintner [9]: m.p. 65-67°.

SUMMARY

The catalytic conversion of butyrolactone into thiophanone-2, pyrrolidone-2, and 1-phenylpyrrolidone-2, effected in the present research, takes place at lower temperatures, though with lower yields, than in the case of furanidine (tetrahydrofuran), owing to the weakening of the butyrolactone ring by the presence of oxygen at the α-carbon atom of the ring.

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Received June 16, 1950

The N.D.Zelinsky Laboratory of Organic Chemistry,
Moscow State University, Awarded the Order of Lenin

XXXVI. THE CONVERSION OF α,β'-DIMETHYLFURAN AND OF α,β'-DIMETHYLFURANIDINE INTO THE CORRESPONDING NITROGEN- AND SULFUR-CONTAINING HETEROCYCLIC COMPOUNDS

Yu.K.Yuryev, G.Ya.Kondratyeva, and A.I.Kartashevsky

In the catalytic conversion of homologs of furanidine (tetrahydrofuran) into the corresponding homologs of pyrrolidine and thiophane the yields of the latter regularly vary with the size of the alkyl radical and its position in the ring.

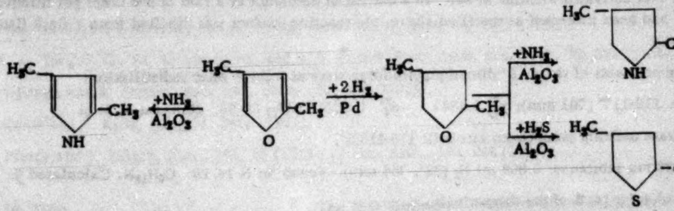
Alkyl radicals located at the α-position weaken the stability of the γ-oxide ring, causing an appreciable drop in the yield of α-alkylpyrrolidines and thiophanes, the magnitude of this effect depending upon the complexity of the alkyl radical. Hence, the reaction is carried out at a lower temperature than that which is best for converting the furanidine, in order to hold down the decomposition of the substance and secure better yields.

In synthesizing α-alkylpyrrolidines at 400°, the yields of α-methyl-[1], α,α'-dimethyl-[2], and α-ethylpyrrolidine [3] were 27.5%, 17.5%, and 9%, respectively, while the yield of pyrrolidine was 46.5% [4]. At 350°, the yield of α-propyl- and α-butylpyrrolidine was 10% [5], whereas the yield of pyrrolidine itself was 30.5% [4]. In synthesizing the α-alkylthiophanes at 350°, the yields of α-methyl- [6], α,α'-dimethyl- [2], α-ethyl-, α-propyl-, and α-butylthiophane [6] were 65%, 43%, 71%, 63% and 60%, respectively, the thiophane yield being 85%, and 90.5% at 400° [7].

When the alkyl radical is located at the β-position of the furanidine ring, the yield of the β-alkylpyrrolidine depends principally upon the size of the radical, the yields of pyrrolidine [4] and β-methylpyrrolidine [5] being 30% at 350°, while the yield of β-butylpyrrolidine was only 12% [5]. The yields of β-methyl, β-ethyl-, β-propyl-, and β-butylthiophane [6] were 81%, 80%, 72%, and 79%, respectively, when the β-alkylthiophanes were synthesized at 350°, i.e., almost the same as the thiophane yield (85%). Hence, the presence of an alkyl radical at the β- position does not affect the stability of the furanidine ring in this reaction.

When homologs of furan are converted into the corresponding homologs of pyrrole and thiophene, the yields of these latter products are likewise reduced, the magnitude of the reduction increasing with increasing size of the alkyl radical located at the α- position of the furan ring.

In the present research we have effected the catalytic conversion of α,β'- dimethylfuran into α, β'- dimethylpyrrole and of α,β'- dimethylfuranidine into α, β'- dimethylpyrrolidine and α,β'-dimethylthiophane.



The yields of these compounds were higher than those of α,α'- dimethylpyrrole (16%), α,α'- dimethylpyrrolidine (17.5%), or α,α'-dimethylthiophane (43%); hence, the yields of the products of this reaction were governed principally by the methyl group located at the α- position of the oxygen-containing heterocyclic ring.

EXPERIMENTAL

α,β'-Dimethylfuran was prepared by using sulfuric acid to condense acetoacetic ester [8], followed by reacting bromine water with the resultant isodehydracetic acid [9] and decarbonizing the resultant α,β'-dimethylfuran-β'-carboxylic acid [10], as well as by a new method we have developed, the pyrolysis of a sultone: the cyclic sulfoether of mesityl oxide [11].

The constants of α,β'-dimethylfuran were as follows after distillation over sodium:

B.p. 93-93.1° (742 mm); n_D^{20} 1.4387; d_4^{20} 0.8996. MR_D 28.08. $C_6H_8O\ulcorner_2$. Calculated MR_D 28.42.

The melting point of the compound with $HgCl_2$ was 111°.

The figures given in the literature for α,β'-dimethylfuran are: Yu. K. Yuryev, G. Ya. Kondratyeva, and S.N. Petrov [11]: b.p. 93-94° (760 mm); n_D^{20} 1.4371; d_4^{20} 0.8993. Gilman and Burtner [12]: m.p. of the compound with $HgCl_2$: 112°.

The α,β'-Dimethylfuranidine (2,4-dimethylfuranidine; 2,4-dimethyltetrahydrofuran) was prepared by hydrogenating α,β'-dimethylfuran catalytically. 40 grams of α,β'-dimethylfuran was passed over palladinized asbestos at 150-155° in a current of hydrogen. The resultant catalyzate was dried with calcium chloride and distilled above sodium in a flask fitted with a tall, highly efficient dephlegmator. The α,β'-dimethylfuranidine's constants were as follows after double distillation:

B.p. 97.5-97.7° (759 mm); n_D^{20} 1.4100; d_4^{20} 0.8433. MR_D 29.57. Calculated MR_D 29.35.

4.350 mg substance: 11.440 mg CO_2; 4.510 mg H_2O. 6.925 mg substance: 18.230 mg CO_2; 7.280 mg H_2O. Found %: C 71.77, 71.84. H 11.61, 11.76. $C_6H_{12}O$. Calculated %: C 71.95; H 12.08.

The yield was 30 g (72% of the theoretical). α,β'-Dimethylfuranidine is not described in the literature.

Conversion of α,β'-dimethylfuran into α,β'-dimethylpyrrole. 9.6 g of α,β'-dimethylfuran was passed over activated alumina at 330° in a current of ammonia at the rate of 5-6 drops per minute. The catalyzate was saturated with sodium hydroxide and extracted with ether. The ether was driven off from the dried ether extract, and the reaction product double-distilled, yielding α,β'-dimethylpyrrole, the constants of which were as follows:

B.p. 165-166° (758 mm); n_D^{20} 1.5048; d_4^{20} 0.9236. MR_D 30.54. $C_6H_9N\ulcorner_2$. Calculated MR_D 30.38.

Picrate melting point (from alcohol) 92.5-93°.

6.250 mg substance: 0.793 ml N_2 (23°, 752 mm). Found %: N 14.48. C_6H_9N. Calculated %: N 14.72.

Yield: 2.4 g (25% of the theoretical).

The figures given in the literature for α,β'-dimethylpyrrole are: Knorr [13]: b.p. 165° (743 mm); Piloty et al [14]: b.p. 162-164° (720 mm); picrate melting point: 92-93°.

Conversion of α,β'-dimethylfuranidine into α,β'-dimethylpyrrolidine. 11.5 g of α,β'-dimethylfuranidine was passed over activated alumina at 300° in a current of ammonia at a rate of 5-6 drops per minute. After the catalyzate had been processed as specified above, the reaction product was distilled from a flask fitted with a dephlegmator.

The constants of the α,β'-dimethylpyrrolidine were as follows after redistillation:

B.p. 116-117° (761 mm); n_D^{20} 1.4347 d_4^{20} 0.8351. MR_D 30.98. Calculated 31.31.

Picrate melting point (from alcohol): 116-116.5°,

6.538 mg substance: 0.806 ml N_2 (22°, 756 mm). Found %: N 14.19. $C_6H_{13}N$. Calculated %: N 14.12.

Yield 4.7 g (41% of the theoretical).

The figures given in the literature for α,β'-dimethylpyrrolidine are: Knorr [13]: b.p. 115-117° (753 mm); n_D^{20} 1.4325; d_4^{20} 0.8297; picrate melting point: 116-117°.

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The resultant α,β'-dimethylthiophane had the following constants:

B.p. 147-148° (742 mm). n_D^{20} 1.4818; d_4^{20} 0.9265. MR_D 35.74. Calculated MR_D 35.68.

Melting point of the compound with $HgCl_2$ (from alcohol): 89°.

7.600 mg substance: 17.270 mg CO_2; 6.810 mg H_2O. 6.310 mg SO_4.
7.980 mg substance: 18.150 mg CO_2; 7.240 mg H_2O. 6.600 mg SO_4.
Found %: C 62.01, 62.07; H 10.03, 10.07; S 27.71, 27.61. $C_6H_{12}S$. Calculated %: C 62.00; H 10.41; S 27.59.

Yield 6.1 g (58.5% of the theoretical). α, β′-Dimethylthiophane has not been described in the literature.

SUMMARY

1. The present paper describes for the first time: a) α, β′-dimethylfuranidine, synthesized by dehydrogenating α,β′-dimethylfuran catalytically with paladinized asbestos; and b) α, β′-dimethylthiophane, synthesized by the catalytic conversion of α, β′-dimethylfuranidine.

2. It has been shown, for the first time, that when α,β′-dimethylfuran and α,β′-dimethylfuranidine are acted upon by ammonia at high temperature in the presence of activated alumina, they are converted into α, β′-dimethylpyrrole and α, β′-dimethylpyrrolidine, respectively. The action of hydrogen sulfide upon α,β′-dimethylfuranidine at 330° in the presence of alumina converts it into α, β′-dimethylthiophane.

3. In the above-described conversion of oxygen-containing heterocyclic compounds into rings containing other hetero atoms, the methyl group located at the β-position of the furan or furanidine ring has no influence on the stability of these rings, provided they possess another methyl group at the α-position: in their behavior in this reaction, α, β′-dimethylfuran and α,β′-dimethylfuranidine most closely resemble α-methylfuran and α-methylfuranidine, respectively, their behavior differing considerably from that of 2,5-dimethylfuran and 2,5-dimethylfuranidine.

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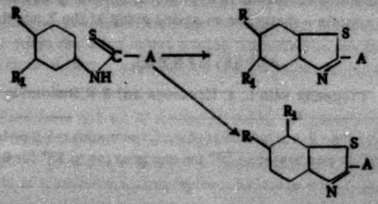
SOME DERIVATIVES OF BENZOTHIAZOLE

III. 2,5,6- and 2,6,7-TRIMETHYLBENZOTHIAZOLES

I. I. Levkoev, N. N. Sveshnikov, N. S. Barvin, and M. P. Pashin

We have previously shown that when meta-substituted thioacetanilides are oxidized, the thiazole ring may be closed at the para as well as at the ortho position to the substituent present in the benzene ring. For instance, when thioacetyl-m-anisidine is oxidized, a mixture of 7- and 5-methoxy-2-methylbenzothiazoles [1] is formed, while oxidation of m-thioacetaminodimethylaniline yields nothing but 7-dimethylamino-2-methylbenzothiazole [2]. Oxidation of thioacetyl-m-nitroaniline has yielded 7-nitro-2-methylbenzothiazole [3].

The 3,4-disubstitution derivatives of thioacetanilide and phenylthiourea can also produce two isomers in this reaction.



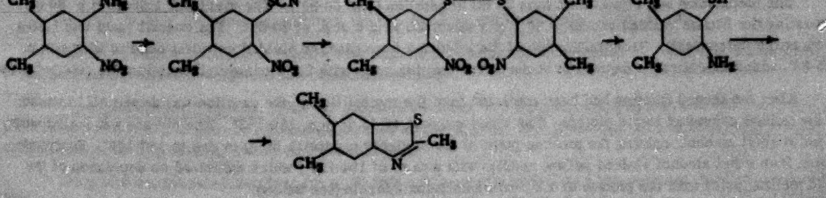
($A = CH_3$ or NH_2).

The closure of the thiazole ring at the ortho position to the second substituent group has not been observed up to the present time, however, in the 3,4-disubstitutition derivatives of thioacetanilide and phenylthiourea. Fries and his co-workers [4] secured only one derivative of benzothiazole – 5,6-dimethoxy-2-methylbenzothiazole – when they oxidized 4-thioacetaminoveratrole. Patents [5] indicate that in the 3,4-diethoxy- and 3-methoxy-4-methylmercaptothioacetanilides the thiazole ring is likewise closed at the para position to the alkoxy group.

We proposed to investigate the ring closure of 3,4-disubstitution derivatives of thioacetanilide and phenylthiourea, using derivatives of 4-amino-1,2-xylene.

Oxidizing 4-thioacetamino-1,2-xylene yielded a mixture of bases that fused in the 30-60° range. Trimethylbenzothiazole, with a m.p. of 85-86°, was recovered from this mixture by means of crystallization.

To establish the structure of this compound we synthesized 2,5,6-trimethylbenzothiazole from 5-amino-4-nitro-1,2-xylene. The latter was converted into 4-nitro-5-thiocyano-1,2-xylene, which was then transformed into 2,2'-dinitro-4,5,4',5'-tetramethyldiphenyl disulfide by treating it with sodium sulfite in aqueous solution (cf [6]). This compound was then reduced with zinc dust in acetic acid, the resulting aminothioxylenol being converted into 2,5,6-trimethylbenzothiazole in the usual manner (cf [7]).



This compound was secured as colorless crystals with a m.p. of 85-86°, which exhibited no depression of the mixed melting point with a previously prepared base.

We have been unable as yet to isolate in a pure state the second base produced when 4-thioacetamino-1,2-xylene is oxidized, owing to its high solubility. It is obvious, however, that a mixture of 2,5,6- and 2,6,7-trimethylbenzothiazole is produced during the process.

We oxidized 3,4-dimethylphenylthiourea with an equimolar quantity of bromine at 0-5° in the presence of chloroform (cf [8]), no perbromides being formed under these conditions. This yielded a mixture of 2-aminodimethylbenzothiazoles, from which we managed to isolate two bases, with m.p. of 185-186° and 198-199°, by means of fractional crystallization, first from methanol and then from ethyl alcohol. When the first of these bases was heated with potassium hydroxide (cf [9]) and the resultant salt of aminothioxylenol then processed with acetic anhydride, it yielded 2,5,6-trimethylbenzothiazole, with a m.p. of 85-86°, so that it was 2-amino-5,6-dimethylbenzothiazole. Similarly, the second base, with a m.p. of 198-199°, produced when 3,4-dimethylphenylthiourea was oxidized must be assigned the structure of 2-amino-6,7-dimethylbenzothiazole. By heating this compound with a concentrated aqueous solution of potassium hydroxide and treating the resulting salt of 2-amino-5,6-dimethylthiophenol with acetic anhydride, we secured 2,6,7-trimethylbenzothiazole as colorless crystals with a m.p. of 40-41°.

Thus, when 3,4-dimethylthioacetanilide and 3,4-dimethylphenylthiourea are oxidized, the thiazole ring is closed at the para and ortho positions to the second methyl group, producing in both cases a mixture of 5,6- and 6,7-dimethylbenzothiazoles that contain a methyl or an amino group at the 2 position.

EXPERIMENTAL

(Together with L. I. Nesterova and E.K.Dudorova)

4-Thioacetylamino-1,2-xylene. A mixture of 16.3 g of 4-acetamino-1,2-xylene, with a m.p. of 97-98° [10], and 11.1 g of phosphorus pentasulfide was heated to 75° for one hour (or to 85° for 30 minutes), causing it to darken and fuse.

The melt was dissolved by heating it with 160 ml of ethyl alcohol, the liquid was cooled, and a solution of 20 g of potassium hydroxide in 600 ml of water was added. The next day, the minute tarry precipitate was filtered out of the solution, and the filtrate was heated to 45° for 30 minutes with activated charcoal. After the charcoal had been filtered out, the solution was neutralized with acetic acid and 4-thioacetylamino-1,2-xylene was thrown down as a yellowish crystalline precipitate by passing carbon dioxide through it. The yield was 8.7 g (49% of the theoretical), m.p. 93-95°. Crystallization from ethyl alcohol raised the melting point to 106-107°. Colorless prisms.

Found %: N 7.75. $C_{10}H_{13}NS$. Calculated %: N 7.82.

When the reaction was carried out in benzene, the yield of 4-thioacetylamino-1,2-xylene (m.p. 99°) was 39% of the theoretical.

Oxidation of 4-thioacetylamino-1,2-xylene. A solution of 17.9 g of 4-thioacetylamino-1,2-xylene (m.p. 93-95°) in 400 ml of 4% sodium hydroxide was gradually added, with vigorous stirring, at 6-8° to a solution of 66 g of potassium ferricyanide in 800 ml of water. Stirring was continued for another hour at the same temperature, after which the reaction product was extracted with ether, the extract dried with potash, the ether driven off, and the residue of 18 g distilled in vacuo, a fraction with a b.p. of 130-143° at 7 mm being collected. The yield was 9.6 g (54.2% of the theoretical), m.p. in the 30-60° range.

The preparation was crystallized from 20 ml of gasoline (b.p. 60-80°). The yield was 1.65 g; m.p. 80-82°. Evaporating the filtrate yielded another 0.20 g of a substance with a m.p. of 80-81°. The overall yield was 1.85 g (10.4% of the theoretical). Recrystallization of the substance from gasoline yielded colorless needles with a m.p. of 85-86°, which exhibited no depression of the mixed melting point with 2,5,6-trimethylbenzothiazole (see below).

After the second fraction had been separated from the mother liquor, the gasoline was driven off in vacuo, and the residue converted into a picrate. The latter weighed 16.15 g; m.p. 150-163°. The picrate was boiled with 320 ml of ethyl alcohol, causing the melting point of the insoluble residue (1.65 g) to rise to 187-190°. Recrystallization from ethyl alcohol yielded yellow needles with a m.p. of 194-195°, which exhibited no depression of the mixed melting point with the picrate of 2,5,6-trimethylbenzothiazole (see below).

The mixture of picrates recovered from the alcoholic solution had a m.p. of 150-165°, which remained practically unchanged after repeated crystallizations.

3,4-Dimethylphenylthiourea. A solution of 48.5 g of potassium thiocyanate in 70 ml of water was added, with stirring, to a solution of 1,2,4-xylidine hydrochloride, prepared by adding 45 ml of hydrochloric acid (sp. gr. 1.19) to a suspension of 60.5 g of the freshly distilled and finely pulverized amine in 300 ml of water. The liquid was heated to 102° (oil temperature) on an oil bath until the water had evaporated (12-14 hours). The dry residue was then heated to 102-105° for 2 hours. The reaction product was triturated with 200 ml of water, the insoluble material being filtered out and washed with 500 ml of water until all the chlorine ion was eliminated. The yield was 78 g (86.7% of the theoretical). M.p. 178-180°. Crystallization from ethyl alcohol raised the product's melting point to 181-182°; this melting point was unchanged by further purification. Colorless needles, fairly readily soluble in alcohol, sparingly soluble in benzene.

Found %: N 15.79, 15.68. $C_9H_{12}N_2S$. Calculated %: N 15.55.

Dyson and George [13], who synthesized 3,4-dimethylphenylthiourea by reacting ammonia with dimethyl phenyl mustard oil or 3,4-dimethylphenylcarbamyl chloride, erroneously give a m.p. of 141.5-142.5° for this compound.

Oxidation of 3,4-dimethylphenylthiourea. A solution of 48 g of bromine in 120 ml of chloroform was gradually added at 0-5°, with vigorous stirring, to a suspension of 54 g of finely powdered 3,4-dimethylphenylthiourea in 270 ml of anhydrous chloroform, causing the evolution of hydrogen bromide. Then the reaction mixture was stirred for another 2 hours at 0-5° and set aside to stand overnight.

The nearly colorless precipitate was filtered out, washed with 200 ml of chloroform, and air-dried. It weighed 87-88 g. The hydrobromide was heated in 1000 ml of water until it dissolved, and the solution was alkalinized with aqueous ammonia. After the solution had cooled, the colorless precipitate was filtered out and washed with water. The yield of the mixture of isomeric dimethyl-2-aminobenzothiazoles totaled 52 g (97% of the theoretical). M.p. 155-160°.

The product was crystallized from 155 ml of methanol, 2-amino-5,6-dimethylbenzothiazole settling out as colorless crystals. Weight: 29 g. M.p. 180-181°. The methanol was driven off from the filtrate and the wash fluids, and the residue (weighing 22.7 g, m.p. 149-152°) was crystallized three times from methanol. Weight 6.55 g; m.p. 181-183°. The total yield of 2-amino-5,6-dimethylbenzothiazole was 35.55 g (66% of the theoretical).

Recrystallization from methanol (1:4) raised the melting point to 185-186°; this m.p. was unaffected by further purification. Colorless needles. Slightly soluble in hot water, rather sparingly soluble in cold benzene, more readily soluble in acetone, and readily soluble in ethyl alcohol and methanol.

Found %: N 15.58, 15.64. $C_9H_{10}N_2S$. Calculated %: N 15.72.

Hydrochloride — colorless crystals (from water). Rather sparingly soluble in water (1:100 at 20°).

Hydrobromide — colorless leaflets (from water).

Sulfate — minute colorless needles (from water). Slightly soluble in water (1:125 at 20°), even less soluble in a 2% solution of potassium sulfate (1:800 at 20°).

All the crystallization mother liquors were combined and evaporated to small volume, the product that settled out being filtered out, dried (weight 12.0 g, m.p. 152-155°), and crystallized three times from 5 parts of ethyl alcohol. This yielded 1.20 g of 2-amino-6,7-dimethylbenzothiazole, m.p. 195-197°. Another recrystallization from ethyl alcohol yielded large, slightly brownish prisms with a m.p. of 198-199°, slightly soluble in hot water, very readily soluble in ethyl alcohol, and extremely soluble in methanol.

Found %: N 15.73: $C_9H_{10}N_2S$. Calculated %: N 15.72.

Hydrochloride — colorless prisms (from water). Slightly soluble in water (1:220 at 20°).

Sulfate — minute colorless crystals. Very slightly soluble in water (1:1000 at 20°) and practically insoluble at ordinary temperatures in a 2% solution of potassium sulfate.

4-Amino-5-nitro-1,2-xylene. This was prepared by nitrating 4-acetamino-1,2-xylene and then saponifying the nitroacetyl derivative with an aqueous solution of an alkali [11]. This procedure yielded better results than the method described by Noelting, Braun, and Thesmar [12].

161 g of 4-acetamino-1,2-xylene (m.p. 97-98°) was gradually added, at a temperature that did not exceed 25°, to 415 ml of sulfuric acid (sp. gr. 1.76), with constant stirring. 64 ml of nitric acid (sp. gr. 1.46) was added drop by drop during the course of 2-2.5 hours at 16-17°, with constant stirring, to the thickened mass. After the

nitric acid had been added, the resulting solution was stirred for another 30 minutes and then poured into a mixture of 6 liters of water and 2 kg of ice. The voluminous yellow precipitate that settled was filtered out and washed successively with water, a weak soda solution, and again with water.

The well-squeezed-out paste (weighing 340 g) was saponified by stirring it for 4 hours at 80-90° with a solution of 42 g of sodium hydroxide in 260 ml of water. When it had cooled to 60°, the precipitated crystals of 4-amino-5-nitro-1,2-xylene were filtered out and washed with warm water until the reaction was neutral.

Crystallization from 6 parts of ethyl alcohol yielded the product as lustrous orange-red prisms with a m.p. of 138-140° (Noelting, Braun, and Thesmar give the m.p. as 139-140° [12]). The yield was 66 g (39.7% of the theoretical).

4-Thiocyano-5-nitro-1,2-xylene. 66.4 g of 4-amino-5-nitro-1,2-xylene was heated to 60-70° with 80 ml of sulfuric acid (sp. gr. 1.84), and the thick mass was poured into a mixture of 800 ml of water and 800 g of ice, the amine sulfate settling out as a fine yellow precipitate. The latter was diazotized by adding a solution of 34.5 g of sodium nitrite in 50 ml of water. After the resultant solution had stood for 30 minutes, it was filtered and a solution of 40.75 g of potassium thiocyanate in 120 ml of water was gradually added, with constant stirring, which immediately precipitated the greenish-yellow thiocyanate. The next day the product was filtered out and washed with water until the reaction was neutral. The yield was 79.5 g (95.6% of the theoretical). M.p. 136-139°.

Yellow orthogonal prisms after a single crystallization from ethyl alcohol, m.p. 141-142°. The product was slightly soluble in ethyl alcohol at ordinary temperatures, though readily soluble when heated in the alcohol; soluble in ether and acetone.

Found %: N 13.37. $C_9H_8O_2N_2S$. Calculated %: N 13.45.

2,2'-Dinitro-4,5,4',5'-tetramethyldiphenyl disulfide. 104 g of 4-thiocyano-5-nitro-1,2-xylene (with a m.p. of 136-139°) was boiled for 4 hours with a solution of 10.15 g of 100% sodium sulfite in 1000 ml of water. The flask was shaken frequently, avoiding all shocks. The next day the product was filtered out and washed with 5 liters of water and with 350 ml of ethyl alcohol. The yield was 85 g, (93.5% of the theoretical). M.p. 206-208°.

Two recrystallizations from benzene raised the melting point to 213-214°. Yellow needles. Slightly soluble in acetone, even less soluble in ethyl alcohol, and nearly insoluble in ether.

Found %: N 7.60. $C_{16}H_{16}O_4N_2S_2$. Calculated %: N 7.69.

2,5,6-Trimethylbenzothiazole. a) From 2,2'-dinitro-4,5,4',5'-tetramethyldiphenyl disulfide. A mixture of 72.8 g of 2,2'-dinitro-4,5,4',5'-tetramethyldiphenyl disulfide (m.p. 206-208°) with 138 g of (100%) zinc dust was gradually added, with stirring, to 600 ml of glacial acetic acid heated to 80-90°. When reduction was complete, the mass was stirred for 30 minutes at 100°. Then 187 g of acetic anhydride was added portionwise, and stirring was continued for another 3 hours at 140-145° (bath temperature). The mass was cooled to 70-80°, diluted with 900 ml of water, and then chilled and alkalinized with a concentrated solution of sodium hydroxide, the resultant base being distilled with steam. The crystalline product was filtered out, pulverized, and washed with water. The yield was 52 g (83.5% of the theoretical), m.p. 82-83.5°.

Two recrystallizations from gasoline (b.p. 60-80°) yielded the product as colorless needles with a m.p. of 85-86°, which remained unaffected by subsequent crystallizations.

Found %: N 7.78. $C_{10}H_{11}NS$. Calculated %: N 7.91.

b) From 2-amino-5,6-dimethylbenzothiazole. A mixture of 14.24 g of 2-amino-5,6-dimethylbenzothiazole with a m.p. of 180-181°, 40 g of potassium hydroxide, and 25 ml of water was heated, with stirring, to 130-135° (temperature of the mass) until no more ammonia was evolved, which usually took 15-18 hours. The mass was slowly cooled, the potassium salt of the aminothioxylenol that settled out being filtered out on a glass filter and thoroughly squeezed out. The salt was then transferred to a three-necked flask fitted with a stirrer and an inclined condenser, and 50 ml of acetic anhydride was gradually added. Then the reaction mass was heated, with stirring, for 3 hours at 180-190° (oil temperature) on an oil bath, 10 ml of acetic acid being driven off. 6 ml of acetic anhydride was added, and the mixture was refluxed for 1 hour. After it had cooled, the mass was diluted with water and alkalinized with a 30% solution of sodium hydroxide, the 2,5,6-trimethylbenzothiazole being driven off with steam. The product was filtered out, washed with water, and dried. The yield was 11-12 g (77-84% of the theoretical). M.p. 80-81°.

Double recrystallization from gasoline (b.p. 60-80°) yielded colorless needles with a m.p. of 85-86°, which exhibited no depression of the mixed melting point with the 2,5,6-trimethylbenzothiazole synthesized by the first method.

Picrate – lustrous yellow needles (from ethyl alcohol), m.p. 194-195°.

The methiodide was secured by refluxing the base for 15 hours with a 50% excess of methyl iodide on a boiling water bath, the yield being 78.9% of the theoretical. Nearly colorless prisms (from ethyl alcohol). M.p. 254-256°.

Found %: N 4.32. $C_{11}H_{14}NSI$. Calculated %: N 4.38.

The ethiodide was similarly prepared from ethyl iodide. Slightly grayish prisms (from ethyl alcohol). M.p. 218-219°.

Found %: N 4.16. $C_{12}H_{16}NSI$. Calculated %: N 4.25.

2,6,7-Trimethylbenzothiazole. 1.78 g of 2-amino-6,7-dimethylbenzothiazole (0.01 mole) was heated, with stirring, with 5 g of potassium hydroxide and 4 ml of water on an oil bath to 135-140° (oil temp.) until no more ammonia was evolved, which usually took 35-40 hours. After the mixture had cooled, the precipitated potassium salt of the aminothioxylenol was filtered out on a glass filter and then transferred to a flask containing 6.5 ml of acetic anhydride. The mixture was stirred and heated for 2 hours witn an inclined condenser on an oil bath at 160-170° (oil temp). Then 2 ml of acetic anhydride was added, and the mixture was refluxed for 1 hour, diluted with water, and alkalinized, the resultant base being distilled with steam. After extraction with ether and drying with potash, the ether was driven off, and the residue (0.70 g) was distilled in vacuo, a fraction with a b.p. of 142-147° at 25 mm being collected. The yield was 0.62 g (35% of the theoretical). Upon cooling the 2,6,7-trimethylbenzothiazole solidified completely into a colorless crystalline mass.

Recrystallization from gasoline yielded the product as large colorless prisms with a m.p. of 40-41°, this melting point remaining unaffected by subsequent crystallizations.

Found %: N 7.90. $C_{10}H_{11}NS$. Calculated %: N 7.91.

Picrate – yellow needles (from ethyl alcohol). M.p. 157-158°.

The methiodide was secured by refluxing the base for 11 hours with a 35% excess of methyl iodide on a water bath, the yield being 69.4% of the theoretical. Nearly colorless prisms (from ethyl alcohol), m.p. 205-206°.

Found %: N 4.21. $C_{11}H_{14}NSI$. Calculated %: N 4.38.

The ethiodide was similarly prepared by refluxing the base for 20 hours with ethyl iodide. The yield was 60% of the theoretical. Nearly colorless prisms (from ethyl alcohol). M.p. 207°.

Found %: N 4.28. $C_{12}H_{16}NSI$. Calculated %: N 4.25.

SUMMARY

1. It has been shown that when 3,4-dimethylthioacetanilide and 3,4-dimethylphenylthiourea are oxidized, the thiazole ring is closed at the ortho and para positions to the methyl group, yielding a mixture of 5,6- and 6,7-dimethylbenzothiazoles, which contain a methyl or an amino group, respectively, at the 2 position.

2. The properties of these bases and of some of their derivatives have been investigated.

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Received June 23, 1950.

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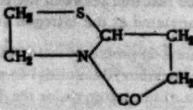
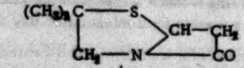
THIAZOLIDINE-4-CARBOXYLIC ACID AND ITS DERIVATIVES

I. THE COMPOUND WITH A THIAZOLIDINE-PYRROLIDONE RING SYSTEM

I. T. Strukov

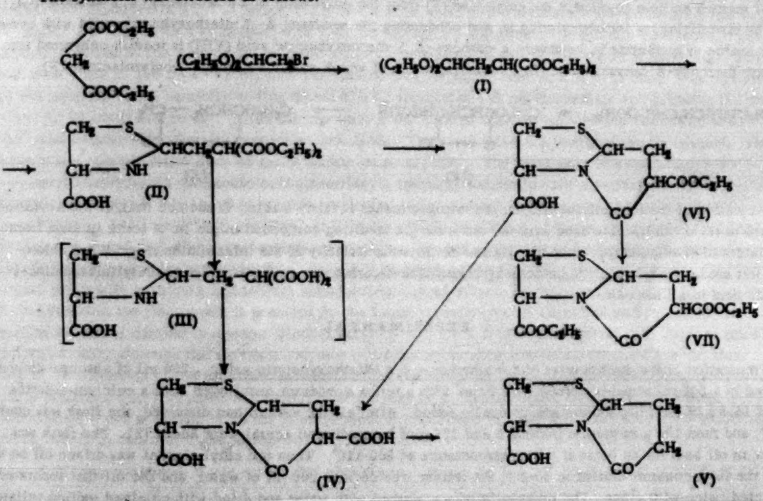
The thiazolidine-pyrrolidone or thiazolidone-γ-lactam ring system is interesting because of its closeness to the thiazolidine-β-lactam system that is the basis of penicillin and its analogs.





This research has been undertaken chiefly to determine how the γ-lactam ring can be closed, using the corresponding substitution derivatives of thiazolidine-4-carboxylic acid, and to make a study of the properties of these compounds.

The synthesis was effected as follows:



Condensing bromodiethyl acetal with malonic ester yielded the ethyl ester of α-carbethoxy-γ,γ-diethoxybutyric acid (I), which yielded the ethyl ester of α-carbethoxy-β-(4-carboxythiazolidyl-2)-propionic acid (II) when heated with l-cysteine hydrochloride. When (I) is heated with cysteine hydrochloride for a long time, the reaction goes further, the compound (II) being converted into the γ-lactam of α-carbethoxy-β-(4-carboxythiazolidyl-2)-propionic acid (VI) and the ethyl ester of this acid (VII).

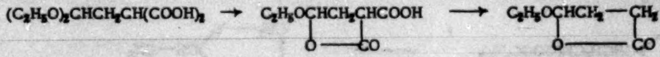
The pyrrolidone (γ-lactam) ring may be closed in a neutral medium as well as by heating the hydrochloride (II); this occurs, for example, when the sodium salt of (II) or the free α-carboxy-β-(4-carboxythiazolidyl-2)-propionic acid (III) is heated. The γ-lactam ring is formed fairly easily.

In aqueous solution the hydrochlorides of 2-substitution derivatives of thiazolidine-4-carboxylic acid are partially hydrolyzed, apparently because of the presence of the adjoining carboxyl group. The primary amino group of cysteine may possess more highly basic properties than the secondary amino group of the thiazolidine ring that is substituted at the 2 position. As a rule, when water is used to dilute the reaction mass produced by condensing cysteine hydrochloride with the ethyl ester of α-carbethoxy-γ,γ-diethoxybutyric acid, a thiazolidine compound is precipitated, though the latter's yield is much higher when the solution is neutralized until its reaction is faintly acid.

Somewhat more iodine is required for the iodometric titration of the sodium salt of (II) than is needed for oxidation, the substance breaking down into cystine and the corresponding aldehyde. This agrees fully with the findings of Ratner and Clarke [1] for thiazolidine-4-carboxylic acid. The iodometric method cannot be employed for the quantitative determination of thiazolidine-4-carboxylic acid or its derivatives because the aldehyde produced in the reaction reacts with the iodine. Inasmuch as the rate at which the cysteine is produced in the cleavage of the thiazolidine ring is much higher than the velocity of the reaction between the iodine and the aldehyde, iodine may be used as a reagent for a thiazolidine ring that is unacylated at the nitrogen atom.

When the γ-lactam of α-carbethoxy-β-(4-carboxythiazolidyl-2)-propionic acid (VI) is saponified with an alkali, it yields the sodium salt of the γ-lactam of α-carboxy-β-(4-carboxythiazolidyl-2)-propionic acid, from which the free acid (IV) may be readily secured. Decarboxylation of the latter yields the γ-lactam of β-(4-carboxythiazolidyl-2)-propionic acid (V). The chemical properties of this compound differ but little from those of the N-acylated thiazolidine-4-carboxylic acids. It is stable in the cold in acid or alkali media, but is broken down rather easily when heated with solutions of caustic alkalies, a thiol group being found in the decomposition products. It hardly reacts with an iodine solution.

It seemed possible to prepare the compound (V) from the ethyl ester of α-carbethoxy-γ,γ-diethoxybutyric acid (I) by saponifying it, decarboxylating it, and condensing the resultant γ,γ-diethoxybutyric acid with cysteine. We were unable to synthesize it, however: α-carboxy-γ,γ-diethoxybutyric acid (VIII) is readily converted into α-carboxy-γ-ethoxy-γ-butyrolactone (IX), decarboxylation of which yields γ-ethoxy-γ-butyrolactone (X):



$$(C_2H_5O)_2CHCH_2CH(COOH)_2 \rightarrow C_2H_5O\underset{O\text{———}}{\underset{|}{C}}HCH_2\underset{CO}{\underset{|}{C}}HCOOH \longrightarrow C_2H_5O\underset{O\text{————}}{\underset{|}{C}}HCH_2\text{—}\underset{CO}{\underset{|}{C}}H_2$$

(VIII) (IX) (X)

Acylation of the thiazolidine ring on the nitrogen makes it fairly stable. It seemed that, if the acylating agent were to set up an instable bond with the nitrogen, the resulting compound might be of some interest from the standpoint of chemotherapy, since diacylation destroys the stability of the thiazolidine ring. Ethyl chloroformate was used for acylation. N-Carbethoxythiazolidine-4-carboxylic acid resembles N-acetylthiazolidine-4-carboxylic acid in all respects.

EXPERIMENTAL

Preparation of the diethyl ester of α-carbethoxy-γ,γ-diethoxybutyric acid. 200 ml of absolute alcohol was placed in a 500-ml round-bottomed flask fitted with a reflux condenser terminated with a calcium-chloride tube, and 14.4 g of metallic sodium was gradually added. After all the sodium had dissolved, the flask was cooled to 40-50°, and then 100 g of diethyl malonate and 128 g of bromodiethyl acetal were added [2]. The flask was heated on an oil bath for 48 hours at a bath temperature of 100-110°. Then the ethyl alcohol was driven off on the oil bath, the flask contents chilled to 15-20°, the residue treated with 200 ml of water, and the oil that separated out extracted twice with ether. The ether solution was washed with water and dried with calcined sodium sulfate, after which the ether was driven off, and the residue fractionated at a 9-mm vacuum.

The ethyl ester of α-carbethoxy-γ,γ-diethoxybutyric acid is a colorless liquid, faintly aromatic, with a b.p. of 146-147° at 9 mm; $[n]_D^{20}$ 1.4275. It is freely soluble in many organic solvents. The yield was 97 g, or 56.5% of the theoretical.

3.574 mg substance: 7.376 mg CO_2; 2.832 mg H_2O. Found %: C 56.28; H 8.87.
$C_{13}H_{24}O_6$. Calculated %: C 56.48; H 8.76.

Preparation of γ-ethoxy-γ-butyrolactone (X). 10 grams of the ethyl ester of α-carbethoxy-γ,γ-diethoxybutyric acid, 30 ml of ethyl alcohol, 20 ml of water, and 7.5 ml of a 29% solution of sodium hydroxide were refluxed for 1 hour. The solution became faintly alkaline. It was concentrated to a thick syrup in vacuo on a water bath. Then 100 ml of ether, 2 ml of concentrated sulfuric acid, and 10 ml of water were added, and the mass was vigorously agitated. The ether solution was decanted. Ether extraction was repeated two more times. Then the ether extract was dried with calcined sodium sulfate, the ether driven off on a water bath, and the residual oil dried in vacuo This yielded 6.5 g of technical α-carboxy-γ-ethoxy-γ-butyrolactone. It is obvious that α-carboxy-γ,γ-diethoxybutyric acid is unstable, being readily converted to the corresponding butyrolactone, alcohol being split off. In direct titration of this acid, 0.1353 g required 7.8 ml of 0.1 N sodium hydroxide solution, equivalent to 100.6%, based on $C_7H_{10}O_5$. The presence of the γ-lactone ring may be established quantitatively by means of back titration. Thus, 16 ml of a 0.1 N sodium hydroxide solution was added to 0.1353 g of the substance, the whole being heated to boiling and left to stand for 18 hours. 0.36 ml of 0.1 N NaOH was back titrated, equivalent to 100.6%, based on the acid $C_7H_{10}O_5$, in which the free and the esterified carboxyl groups were back-titrated.

The α-carboxy-γ-ethoxy-γ-butyrolactone was decarboxylated on an oil bath at 150° until no more carbon dioxide was evolved. The residue was fractionated in vacuo, yielding a fraction with a b.p. of 88-90° at 10 mm. A colorless liquid with the odor of stearin, freely soluble in alcohol, ether, and ethyl acetate, and insoluble in water.

3.642 mg substance: 7.953 mg CO_2; 2.570 mg H_2O. 5.116 mg substance: 10.161 mg CO_2; 3.638 mg H_2O. Found %: C 55.31, 55.16; H 7.89, 7.95. $C_6H_{10}O_3$. Calculated %: C 55.35; H 7.75.

The substance contained a lactone group, disclosed by back-titration after it had been heated with a sodium hydroxide solution. 20 ml of 0.1 N NaOH was added to 0.1068 g of the substance, and the mixture was refluxed for 1 hour. After the mixture had cooled, 11.7 ml of 0.1 N NaOH was back-titrated, equivalent to 100.9%, based on γ-ethoxy-γ-butyrolactone ($C_6H_{10}O_3$).

Ethyl ester of α-carbethoxy-β-(4-carboxythiazolidyl-2)-propionic acid (II). 5 g of l-cysteine hydrochloride was dissolved in 2 ml of water, 8.5 g of the ethyl ester of α-carbethoxy-γ,γ-diethoxybutyric acid was added, and the whole was heated, with vigorous stirring, on a boiling water bath for 10 minutes. The emulsion produced at the start of the reaction quickly disappeared, a yellow homogeneous mass being formed. It was transferred to 100 ml of water, with constant stirring, crystallization setting in at once. The hydrochloric acid was neutralized by carefully adding 23 ml of a 5% solution of sodium bicarbonate and allowing the mass to stand for 24 hours at 0 to +2°. Then the precipitate was filtered out, washed with ice water, dried at 30-40°, and washed with ether in a separate little flask. The yield was 6.5 g or 68% of the theoretical. The substance was recrystallized from 40 ml of water; m.p. 124-125°. The ethyl ester of α-carbethoxy-β-(4-carboxythiazolidyl-2)-propionic acid (lamellae) is sparingly soluble in cold water and freely soluble in hot water, sparingly soluble in ether, soluble in alcohol, ethyl acetate, acetone, and chloroform, hardly soluble in benzene, and insoluble in gasoline; it is freely soluble in alkalies. When a 4% aqueous solution of the sodium salt is stored, the substance decomposes, yielding hexahedral crystals of l-cystine, the odor of acetaldehyde malonic ester being perceptible. A freshly prepared aqueous solution does not exhibit a reaction for the thiol group with ammonia and sodium nitroprusside, though after it has been heated with a 5% solution of sodium hydroxide the thiol group is revealed by the bright crimson color produced by sodium nitroprusside. When the Na salt is titrated in a water-alcohol medium with a 0.1 N solution of iodine, the latter is quickly decolorized, and, although the titration endpoint is readily detectable, the results obtained are too high, owing to the oxidation of the aldehyde produced during the reaction. When the titrated solution is allowed to stand, a precipitate of l-cystine soon begins to settle out; m.p. 220-222° (true hexagonal lamellae). 0.700 g of the substance was dissolved in 20 ml of ethyl alcohol and back-titrated with 2.3 ml of 0.1 N NaOH, equivalent to 100.5% in terms of $C_{12}H_{19}O_6NS$.

6.027 mg substance: 0.244 ml N_2 (21°, 746.5 mm). Found %: N 4.62. $C_{12}H_{19}O_6NS$. Calc.%: N 4.59.

Cleavage of the thiazolidine ring by mercuric chloride. 1 g of the ethyl ester of α-carbethoxy-β-(4-carboxythiazolidyl-2)-propionic acid, 0.9 g of mercuric chloride, and 10 ml of methanol were rapidly stirred, causing dissolution at first, though the solution quickly began to turn cloudy, a white crystalline complex salt of cysteine and mercuric chloride settling out. To complete cleavage, we added 1 ml of water, shook the mixture up, and allowed it to stand for 1 hour. Then the precipitate was filtered out, and the filtrate evaporated in vacuo to dryness. The crystalline residue was treated with 50 ml of ether, the acetaldehyde malonic ester dissolving and the solution being filtered to free it of the precipitate. The precipitate weighed about 1.3 g. The ether solution was washed with 10 ml of 2 N HCl, and then twice with water, after which it was dried with a calcined sodium sulfate and the ether driven off. This left 0.5 g of a light-yellow liquid, which reduced silver from a complex ammoniacal silver salt.

γ-Lactam of α-carbethoxy-β-(4-carboxythiazolidyl-2)-propionic acid (VI). 2.6 ml of a 20% alcoholic solution of sodium hydroxide (in methanol) was added to 4 g of the ethyl ester of α-carbethoxy-β-(4-carboxythiazolidyl-2)-propionic acid in 30 ml of methanol. The acid dissolved. The reaction must be neutral and not alkaline. The methanol was driven off, the residue being heated on a boiling water bath for 4 hours. This produced a yellow hyaline mass, which dissolved completely in 30 ml of water. The substance settling out when the solution was acidulated with 2 ml of 40% sulfuric acid, was extracted with ethyl acetate. The ether extract was washed with 8 ml of 40% sulfuric acid, washed twice with water, and dried with calcined sodium sulfate. The ethyl acetate was driven off, and the remaining light-yellow oil dried in a 10-mm vacuum on a boiling water bath, yielding 2.7 g of the substance.

A very thick, light-yellow oil, insoluble in water and freely soluble in alcohol, ether, chloroform, benzene, and a sodium hydroxide solution. The potential thiol group was disclosed by a reaction with sodium nitroprusside after the substance had been heated for 1-2 minutes with a 20% solution of sodium hydroxide. The solution decolorized iodine extremely slowly. Titration with a 0.1 N solution of sodium hydroxide in an alcoholic solution yielded 101.1% and 101.3%, based on $C_{10}H_{13}O_5NS$ as a monocarboxylic acid.

0.3340 g substance: 0.2900 g $BaSO_4$. 0.3140 g substance: 0.2718 g $BaSO_4$. 6.000 mg substance: 2.40 ml 0.01 N H_2SO_4. Found %: S 11.92, 11.88; N 5.60. $C_{10}H_{13}O_5NS$. Calc. %: S 12.35; N 5.40.

γ-Lactam of α-carboxy-β-(4-carboxythiazolidyl-2)-propionic acid (IV). 15 g of the γ-lactam of α-carbethoxy-β-(4-carboxythiazolidyl-2)-propionic acid was dissolved in 100 ml of methanol, and 23 g of a 20% solution of sodium hydroxide in methanol was added. A crystalline precipitate of the sodium salt soon began to settle out. The reaction mass was refluxed for 6 hours at 50-60° to complete saponification. After the mass had cooled, the precipitate was filtered out, washed twice with a small quantity of cold methanol, and dried in a vacuum desiccator. This yielded 11.2 g of the sodium salt—a light-yellow powder that blazed brightly. The salt was hygroscopic.

Found %: Na 16.4. $C_8H_7O_5NSNa_2$. Calculated %: Na 16.73.

10 g of the resultant sodium salt was treated with 20 ml of 25% sulfuric acid, the dicarboxylic acid produced being extracted eight to ten times with ether. The ether solution was dried with calcined sodium sulfate, and the ether was driven off until the volume totaled 10-15 ml. As the ether evaporated, large crystals soon began to settle out in the crystallizer; they were filtered out and washed with a small quantity of ether. The yield was 3.6 g. Large prisms from an acetone-benzene mixture, m.p. 134-135° (with decomp.), freely soluble in water, acetone, alcohol, and ethyl acetate, sparingly in ether, and insoluble in benzene. The potential thio group was detected in the same way as for the compound (VI). It reacted very slowly with an iodine solution. Titration with 0.1 N solution of sodium hydroxide yielded 99.0-99.1%, based on the dicarboxylic acid $C_8H_9O_5NS$.

5.713 mg substance: 0.289 ml N_2 (21.7°, 751 mm). Found %: N 5.8. $C_8H_9O_5NS$. Calc. %: N 6.06.

γ-Lactam of β-(4-carboxythiazolidyl-2)-propionic acid (V). When the γ-lactam of α-carboxy-β-(4-carboxythiazolidyl-2)-propionic acid was heated to 130-140° at a vacuum of 10 mm for 1.5 hours in a Würtz flask, CO_2 was liberated. The residual yellow oil quickly crystallized upon cooling. The γ-lactam was recrystallized from 1:3 acetone. Large prisms with a m.p. of 137-137.5°, freely soluble in water, alcohol, and acetone, less so in ethyl acetate, ether, and chloroform, and insoluble in benzene. An aqueous solution reacts very slowly with iodine. The potential thiol group was detected as in the case of the compound (VI). It titrated as a monocarbowylic acid with a 0.1 N solution of NaOH, yielding 99.2-99.5%, based on $C_7H_9O_3NS$.

8.023 mg substance: 4.36 ml 0.01 N H_2SO_4 8.151 mg substance: 4.38 ml 0.01 N H_2SO_4. Found %: N 7.61, 7.53. $C_7H_9O_3NS$. Calculated %: N 7.49.

The compound (V) does not precipitate a complex salt of cysteine and $HgCl_2$ when treated with a solution of mercuric chloride, which is evidence of the stability of the thiazolidine ring when acetylated on nitrogen.

γ-Lactam of α-carbethoxy-β-(4-carbethoxythiazolidyl-2)-propionic acid (VII). This compound was readily produced by heating l-cysteine hydrochloride for 2 hours with the ethyl ester of α-carbethoxy-γ,γ-diethoxybutyric acid. Small quantities of the compound (VI) were produced at the same time, which indicates how easily the carboxyl group of the thiazolidine ring can be esterified.

5 g of cysteine hydrochloride was heated, with stirring, for 2 hours with 8.5 g of the ethyl ester of α-carbethoxy-γ,γ-diethoxybutyric acid. The resultant thick yellow oil was treated with 50 ml of ether and 20 ml of water. The ether solution was separated, washed (while shaken vigorously) with 10 ml of 40% sulfuric

acid, and then with 20 ml of a 5% solution of sodium bicarbonate and with water, and dried with calcined sodium sulfate. The ether solution was filtered, and the ether driven off on a water bath. The residual ether was eliminated in vacuo, leaving behind a thick, non-crystallizing, light-yellow oil; it was insoluble in water, though freely soluble in alcohol, ether, acetone, and chloroform. The potential thiol group was detected as indicated above. It reacts hardly at all with iodine in an alcoholic solution. Saponification yields the compound (IV) with a m.p. of 132-134° (with decomp.).

Found %: N 5.01, 4.9 $C_{12}H_{17}O_5NS$. Calculated %: N 4.87.

N-Carbethoxythiazolidine-4-carboxylic acid. 3 g of the calcium salt of thiazolidine-4-carboxylic acid, 30 ml of water, and 2 g of ethyl chloroformate were agitated together for 5 minutes. The calcium salt dissolved, the liquid becoming transparent. The next day the solution was evaporated in vacuo on a water bath. The residue was processed with ether, the ether solution being dried with calcined sodium sulfate and filtered. Large octahedra formed when the ether was slowly evaporated. They were filtered out and washed with a small amount of anhydrous ether. The yield was 2.5 g; m.p. 96-97°. The substance is very soluble in hot water, alcohol, ether, benzene, chloroform, and ethyl acetate, and insoluble in gasoline. It does not decolorize an iodine solution. It does not produce a complex salt of cysteine and mercuric chloride when reacted with a solution of $HgCl_2$, which is evidence that the thiazolidine ring is stabilized by the presence of a carbethoxy group attached to the nitrogen atom.

Titration of 0.1035 g of the substance with a 0.1 N solution of sodium hydroxide used up 5 ml of the alkali, equivalent to 99.01%, based on N-carbethoxythiazolidine-4-carboxylic acid.

3.571 mg substance: 0.214 ml N_2 (20°, 744 mm). 7.261 mg substance: 0.446 ml N_2 (24.5°, 712 mm). Found %: N 6.82, 6.87. $C_7H_{11}O_4NS$. Calculated %: N 6.82.

SUMMARY

1. Several thiazolidine-pyrrolidone-carboxylic compounds have been synthesized from l-cysteine hydrochloride and the diethyl ester of β, β-diethoxyethylmalonic acid.

2. N-Carbethoxythiazolidine-4-carboxylic acid has been synthesized.

The physical and chemical properties of these compounds resemble those of the N-acylthiazolidine-4-carboxylic acids.

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Received July 8, 1950

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1

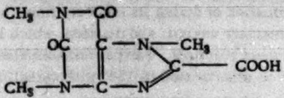
THE 8-SUBSTITUTION DERIVATIVES OF METHYLATED XANTHINES

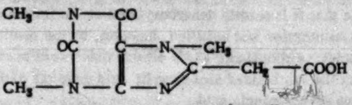
II. SYNTHESIS OF β-(CAFFEINE-8)-PROPIONIC ACID

E. S. Golovchinskaya and E. S. Chaman

In a previous report [1], one of the present authors has described caffeine-8-aldehyde. This compound is formed, with a high yield, from 8-methylcaffeine [2]. The use of caffeine-8-aldehyde as a raw material has opened up extensive prospects for the synthesis of various derivatives of caffeine, especially monobasic and dibasic aliphatic acids with three-membered carbon chains, substituted at the 8 position.

Only very few caffeine derivatives substituted at the 8 position are known at the present time. Two representatives of this group are known: caffeine-8-carboxylic acid [3] and caffeine-8-acetic acid [4]:

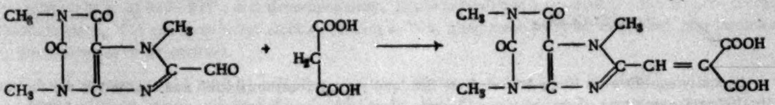




Both of these acids are highly unstable; they are readily decarboxylated, being converted into caffeine and 8-methylcaffeine, respectively. There are no descriptions in the literature of compounds with elongated chains or of unsaturated and dibasic acids of this series.

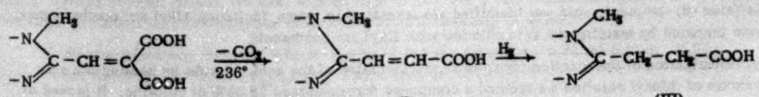
It might have been supposed that lengthening the aliphatic chain and, hence, increasing the distance between the carboxylic group and the caffeine ring would diminish the influence of the latter upon that group, thus producing more highly stable compounds. In the patent literature there is a description of a method for preparing methylated derivatives of xanthine-8-carboxylic acids, involving the acylation of 2,6-dihydroxy-4,5-diaminopyrimidine and its methylated homologs with dicarboxylic aliphatic acids [5]. Closure of the imidazole ring in the resultant acylated diamines leads to the formation of xanthine, as well as mono- and dimethylxanthine, with an aliphatic acid substituted at the 8 position. This method was employed to synthesize theophylline-8-propionic acid and other compounds. Further methylation of these acids would apparently have yielded the corresponding derivatives of caffeine. This cumbersome and complicated reaction pattern does not profide satisfactory yields of the end product, whereas synthesis employing caffeinaldehyde ensures high yields in every stage of the process.

The first stage of this synthesis — condensing caffeinaldehyde with malonic acid in glacial acetic acid — results in the formation of caffeine-8-methylenemalonic acid (I):



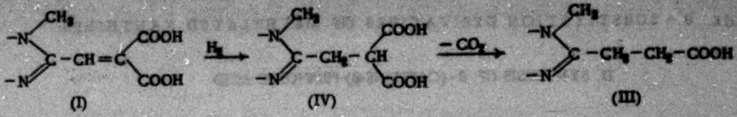
(I)

This acid proved to be a rather stable compound, carbon dioxide being split out only upon fusion (236°), which converted the acid into β-(caffeine-8)-acrylic acid (II). Hydrogenating the latter yielded β-caffeine-8-propionic acid (III):



(I) (II) (III)

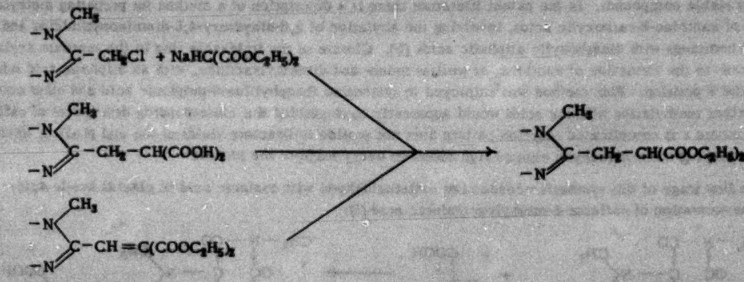
Another possible synthesis procedure involves the preliminary hydrogenation of caffeine-8-methylenemalonic acid, followed by decarboxylation of the resultant caffeine-8-isosuccinic acid (IV):



High yields of β-caffeinepropionic acid were secured by both methods. Partial decarboxylation of caffeinemethylenemalonic acid and hydrogenation with Raney's nickel of an aqueous solution of the sodium salt of the caffeineacrylic acid (II) prepared from it yielded an extremely stable crystalline substance with a m.p. of 232-233°, β-(caffeine-8)-propionic acid (III), which we were unable to decarboxylate, either by heating it above its melting point or even by heating it to high temperatures with quinoline. Hydrogenating the sodium salt of caffeinemethylenemalonic acid under the same conditions yielded an acid with a m.p. of 230-232°, which gave off no carbon dioxide even when heated to 250-260° and greatly resembled β-(caffeine-8)-propionic acid in appearance and in solubility in water and organic solvents. The mixed melting point of these two acids exhibited no depression.

The unexpected similarity in the physicochemical properties of these two compounds and the absence of any depression of their mixed melting point led us at first to believe that the saturated dicarboxylic acid (IV) is so unstable that it is readily decarboxylated at the instant of its formation or during its recovery from its sodium salt. This assumption was nullified, however, by the results of elementary analysis and titration, which bore out that two acids — a monobasic and a dibasic one — were produced in these reactions. Further research also demonstrated that the synthesized dicarboxylic acid gave off carbon dioxide when heated to 130° with quinoline, yielding β-(caffeine-8)-propionic acid.

There was a considerable difference between the melting points of the ethyl esters of these two acids, and their mixed melting point exhibited a marked depression. The diethyl ester of caffeine-8-isosuccinic acid, with a m.p. of 101°, was likewise synthesized by reacting 8-chloromethylcaffeine with sodium malonic ester in absolute toluene. This ester proved to be the same as the ester of the dicarboxylic acid described above, and as the ester produced by hydrogenating the diethyl ester of caffeine-8-methylenemalonic acid (I).



Saponifying this ester in an acid medium involved partial decarboxylation and resulted in the formation of β-(caffeine-8)-propionic acid, while esterification of the latter yielded the ester with an m.p. of 136°.

These reactions showed the caffeine-8-isosuccinic acid was an extraordinarily stable compound, in contrast to other dicarboxylic acids with two carboxylic groups on a single carbon atom. They likewise constituted a rather rare instance of the absence of depression of the mixed melting point of two distinct, though related, compounds, whose properties and melting points happen to coincide.

β-(Caffeine-8)-propionic acid was identified via several of its esters, including alkyl aminoethyl esters. The latter were prepared by reacting the acid chloride with alkyl aminoethanols.

In our investigation of the reaction involved in the formation of the acid chloride by heating the acid with a large excess of thionyl chloride we secured a compound that contained 29.55% of chlorine. It proved to be β-(caffeine-8)-dichloropropionyl chloride, with both of the chlorine atoms in the side chain. The only way we could secure the acid chloride of the acid unsubstituted by chlorine was by cautiously heating the acid with a slight excess of thionyl chloride (8-10%) in absolute benzene. This acid chloride proved to be so unstable that we could not purify it for analysis, inasmuch as it was partially hydrolyzed during crystallization, even from absolute benzene. Still there is no doubt about the structure of the acid chloride, since the action of ammonia upon it produced a nearly quantitative yield of an amide that was the same as the amide formed from the methyl ester of β-(caffeine-8)-propionic acid when reacted with aqueous ammonia.

The authors wish to express their heartfelt gratitude to Prof. O. Yu. Magidson for his interest in the present research.

EXPERIMENTAL

(Caffeine-8)-methylenemalonic acid. 44.7 g of 8-caffeinaldehyde, 23 g of malonic acid (prepared by the V. M. Rodionov and A. A. Zvorykina method [6]), and 75 ml of glacial acetic acid were stirred together while heated to 90-95° on a water bath for 5 hours. The cooled reaction mass was filtered, the precipitate being washed with glacial acetic acid and ether and then dried. The yield was 51 g, or 82% of the theoretical. The product was crystallized from 1:60 glacial acetic acid. A yellow powder with an m.p. of 235-236° (with decomposition), insoluble in water, alcohol, chloroform, and other organic solvents, and soluble in a solution of $NaHCO_3$, giving off CO_2. It settles out of an acidulated aqueous solution of the sodium salt in linked clusters of minute needles.

6.280 mg substance: 8.22 ml 0.01 N H_2SO_4. 5.132 mg substance: 6.67 ml 0.01 N H_2SO_4. Found %: N 18.35, 18.39. $C_{12}H_{12}O_6N_4$. Calculated %: N 18.18.

Diethyl ester of (caffeine-8)-methylenemalonic acid. 3 grams of (caffeine 8)-methylenemalonic acid was heated on a boiling water bath for 6 hours with a mixture of 50 ml of absolute ethyl alcohol and 1 g of sulfuric acid (1.84). As the mixture cooled, 1.85 g of the ester, with an m.p. of 181-183°, crystallized out. Another 0.35 g of the ester was recovered from the filtrate by the usual procedures. The yield totaled 2.2 g, or 62% of the theoretical. The ester was crystallized from alcohol (1:10) for analysis. Faintly yellowish-green minute silky needles with an m.p. of 183-184°.

6.708 mg substance: 7.33 ml 0.01 N H_2SO_4. 6.435 mg substance: 7.13 ml 0.01 N H_2SO_4. 3.531 mg substance: 6.835 mg CO_2; 1.678 mg H_2O. Found %: C 52.79; H 5.31; N 15.39, 15.49. $C_{16}H_{20}O_6N_4$. Calculated %: C 52.75; H 5.49; N 15.39.

β-(Caffeine-8)-acrylic acid. 1.5 grams of (caffeine-8)-methylenemalonic acid was heated for 50-60 minutes with 7 ml of quinoline at a bath temperature of 150-160°. The caffeinacrylic acid that settled out upon cooling was filtered and washed with dilute HCl and with water. Then it was dissolved in a solution of $NaHCO_3$ and precipitated by acidulating the solution. The yield was 0.7 g. The quinoline filtrate was agitated 2 or 3 times with a $NaHCO_3$ solution. The bicarbonate solution was washed repeatedly with diethyl ether and then acidulated with hydrochloric acid (1.19) until its reaction was faintly acid with Congo red. This yielded another 0.1 g of the caffein-acrylic acid. The total yield was 0.8 g, or 62.5% of the theoretical. A yellow, finely crystalline substance, with an m.p. of 269-271° (with decomposition). It was crystallized from methyl ethyl ketone (1:100), from chlorotoluene (1:120) and from butyl alcohol (1:160), as thin, transparent, rhombic lamellae. It is insoluble in water, ethyl alcohol, or chloroform.

4.544 mg substance: 6.85 ml 0.01 N H_2SO_4. 3.621 mg substance: 5.46 ml 0.01 N H_2SO_4. Found %: N 21.10, 21.11. $C_{11}H_{12}O_4N_4$. Calculated %: N 21.21.

Ethyl ester of β-(caffeine-8)-acrylic acid. 2 grams of caffeinacrylic acid was heated for 6 hours with a mixture of 80 ml of absolute ethyl alcohol and 0.5 g of sulfuric acid (1.84). After the solution had cooled, 1.9 g of the ester crystallized out. The filtrate was processed in the usual manner, yielding another 0.2 g of the ester. The ester was purified by crystallizing it from alcohol. The total yield was 2.0 g (90% of the theoretical). Faintly colored minute needles, with an m.p. of 207-208°, very soluble in chloroform. It crystallizes from alcohol, carbon tetrachloride, and ethyl acetate. It is insoluble in water.

5.386 mg substance: 7.40 ml 0.01 N H_2SO_4. 7.015 mg substance: 9.54 ml 0.01 N H_2SO_4. Found %: N 19.23, 19.04. $C_{13}H_{16}O_4N_4$. Calculated %: N 19.17.

β-(Caffeine-8)-propionic acid. 0.5 gram of caffeinacrylic acid was dissolved in 18.8 ml of 0.1N NaOH, 0.5 g of a Raney nickel catalyst was added, and the solution was hydrogenated at room temperature for 45 minutes, with mechanical stirring, 45 ml of hydrogen being absorbed. The reaction mass was filtered, the catalyst washed with 1-2 ml of water, and the combined filtrate and wash water was acidulated with hydrochloric acid (1.19) until its reaction was slightly acid with Congo red. 0.48 gram (96% of the theoretical) of caffeinepropionic acid gradually settled out. A white, finely crystalline substance with an m.p. of 232-233°. It crystallized as minute needles from water, methanol (1:35), and ethyl alcohol (1:40). It is insoluble in benzene or chloroform.

0.3366 g substance: 12.77 ml 0.1 N NaOH. Calculated: 12.65 ml 0.1 N NaOH. 5.387 mg substance: 8.10 mg 0.01 N H_2SO_4. 5.878 mg substance: 8.87 mg 0.01 N H_2SO_4. Found %: N 21.05, 21.12. $C_{11}H_{14}O_4N_4$. Calculated %: N 21.05.

Ethyl ester of β-(caffeine-8)-propionic acid. 2 grams of caffeinepropionic acid was heated for 4 hours with a mixture of 30 ml of absolute ethyl alcohol and 0.5 g of H_2SO_4 (1.84). The alcohol was then driven off, and the residue was treated with ice water, the ester being precipitated with anhydrous $NaHCO_3$ and extracted with chloroform. The ester yield was 1.8 g (81% of the theoretical). White lamellae with an m.p. of 135-136°, very soluble in chloroform, and insoluble in water. The ester crystallizes from alcohol.

5.919 mg substance: 7.97 ml 0.01 N H_2SO_4. 5.876 mg substance: 7.91 ml 0.01 N H_2SO_4. Found %: N 18.85, 18.91. $C_{13}H_{18}O_4N_4$. Calculated %: N 19.05.

Hydrogenating the ethyl ester of β-(caffeine-8)-acrylic acid. A suspension of 0.5 g of the ethyl ester of caffeinacrylic acid in 100 ml of ethyl alcohol was hydrogenated for 40 minutes at room temperature, with mechanical stirring, with 0.5 g of Raney nickel catalyst, 45 ml of hydrogen being absorbed. The catalyst was filtered out, and the alcohol driven off. The ethyl ester of β-(caffeine-8)-propionic acid has an m.p. of 132-133°. The yield was 0.48 g (95% of the theoretical).

Methyl ester of β-(caffeine-8)-propionic acid. 25 grams of caffeinepropionic acid was heated for 4 hours with a mixture of 300 ml of absolute methanol and 5 g of H_2SO_4 (1.84). The ester yield was 23 g (87% of the theoretical). The ester was purified by crystallizing it from 1:10 methanol and ethyl alcohol. Minute white needles with an m.p. of 162-164°.

5.872 mg substance: 8.39 ml 0.01 N H_2SO_4. 5.985 mg substance: 8.60 ml 0.01 N H_2SO_4. Found %: N 20.00, 20.12. $C_{12}H_{16}O_4N_4$. Calculated %: N 20.00.

Sodium β-(caffeine-8)-propionate. An alcoholic solution of NaOH was added to a heated and stirred solution of 5 g of caffeinepropionic acid in 200 ml of absolute alcohol until the reaction with phenolphthalein was slightly alkaline. The solution was stirred for an hour and a half and then allowed to stand overnight. A crystalline precipitate settled out slowly. The solution was heated to boiling and rapidly filtered while hot. The yield was 4 g, or 74% of the theoretical. Driving off the alcohol, dissolving the residue in water, and acidulating the solution yielded 1.1 g of the initial acid. The salt consisted of minute white needles with an m.p. of 280-288° (with decomposition), freely soluble in water and insoluble in organic solvents.

4.675 mg substance: 6.40 ml 0.01 N H_2SO_4. 5.820 mg substance: 8.01 ml 0.01 N H_2SO_4. Found %: N 19.20, 19.28. $C_{11}H_{13}O_4N_4Na$. Calculated %: N 19.44.

(Caffeine-8)-isosuccinic acid. 50 grams of (caffeine-8)-methylenemalonic acid was dissolved in 325 ml of 1N NaOH, and 10 g of a Raney nickel catalyst was added. Hydrogenation lasted 6 hours at room temperature, with mechanical agitation, 3690 ml of hydrogen being absorbed. The reaction mass was filtered, the catalyst washed with water, and the combined filtrate and wash water acidulated with hydrochloric acid (sp. gr. 1.19) until the reaction with Congo red was slightly acid. A coarse crystalline precipitate slowly settled out upon standing. The yield was 48 g (96% of the theoretical). Transparent crystals with an m.p. of 230-232°, freely soluble in alcohol. It crystallized from water (1:30) as colorless, square, lamellae. When a solution of the sodium salt was acidulated, the acid settled out as large rhombic lamellae. Insoluble in benzene, acetone, ethyl acetate, or chloroform.

5.309 mg substance: 6.85 ml 0.01 N H_2SO_4. 5.00 mg substance: 6.40 ml 0.01 N H_2SO_4. Found %: N 18.06, 17.92. $C_{12}H_{14}O_6N_4$. Calculated %: N 18.06.

Diethyl ester of β-(caffeine-8)-isosuccinic acid. 4 grams of β-(caffeine-8)-isosuccinic acid was heated for 4 hours with a mixture of 60 ml of absolute ethyl alcohol and 1 g of H_2SO_4 (1.84). The ester yield was 3.6 g (76.0 % of the theoretical.). Transparent prisms with an m.p. of 101 - 102°, soluble in the cold in benzene and chloroform. It crystallized from 1:2 alcohol and from 1:80 water. It is insoluble in ether.

7.76 mg substance: 8.43 ml 0.01 N H_2SO_4. 7.43 mg substance: 8.08 ml 0.01 N H_2SO_4.
Found %: N 15.21, 15.21. $C_{16}H_{22}O_6N_4$. Calculated %: N 15.30.

Hydrogenating the diethyl ester of β-(caffeine-8)-methylenemalonic acid. A suspension of 0.5 g of the ester in 150 ml of ethyl alcohol plus 0.5 g of Raney nickel catalyst was hydrogenated for 45 minutes at room temperature, with mechanical stirring, 45 ml of hydrogen being absorbed. The m.p. of the resultant diethyl ester of β-(caffeine-8)-isosuccinic acid was 101-102°. The yield was 0.47 g (94% of the theoretical.).

Condensing 8-monochloromethylcaffeine with sodium malonic ester. A suspension of 0.5 g of finely divided sodium in 30 ml of absolute toluene was stirred while 6.4 g of the malonic ester was added. After the metallic sodium had vanished, the reaction mixture was cooled to 20-40°, and 4.8 g of thoroughly pulverized anhydrous 8-monochloromethylcaffeine was added, after which heating was resumed for 1 hour. The toluene was then driven off in vacuo. The crystallized residue weighed 6 g, with an m.p. of 98-100°. The yield was 82% of the theoretical. The ester was purified by crystallizing it from water. The ester was identical with the diethyl ester of β-(caffeine-8)-isosuccinic acid, synthesized by esterifying the acid and by hydrogenating the ester of (caffeine-8)-methylenemalonic acid.

Decarboxylating β-(caffeine-8)-isosuccinic acid. 10 grams of β-(caffeine-8)-isosuccinic acid was heated to 130° with 45-50 ml of quinoline. The caffeinepropionic acid that crystallized out upon cooling was filtered out and thoroughly washed with dilute HCl and with water. It was purified by dissolving it in a solution of $NaHCO_3$, filtering the solution, and then acidulating the solution of the sodium salt. The yield was 7.85 g (91% of the theoretical).

Saponifying and decarboxylating the diethyl ester of β-(caffeine-8)-isosuccinic acid. 5 grams of the diethyl ester of (caffeine-8)-isosuccinic acid was boiled for 4.5 hours with 50 ml of dilute (1:1) HCl. The hot solution was decolorized with charcoal, filtered, and cooled, after which the chilled solution was neutralized, first with an alkali solution, and then with anhydrous $NaHCO_3$ until its reaction with Congo red was faintly acid. The precipitated caffeinepropionic acid was purified in the usual manner. The yield was 3.5 g (95.5% of the theoretical.).

Preparation of β-(caffeine-8)-propionyl chloride. 2 grams of the anhydrous acid was heated with 15 ml of absolute benzene and 1 g of thionyl chloride* and stirred until all the acid had dissolved at the boiling point of benzene. Upon cooling, yellow crystals with an m.p. of 127-135° adhered to the walls of the flask. The yield was 1.5 g (70% of the theoretical). The benzene mother liquor was processed with 20 ml of 25% aqueous ammonia, yielding 0.35 g of caffeinepropionamide, with an m.p. of 229-232° (see below).

β-(Caffeine-8)-propionamide. a) A mixture of 20 g of caffeinepropionic acid, 150 ml of absolute benzene, and 10 g of thionyl chloride was stirred and heated for 3-4 hours until all the acid had dissolved. The resultant solution of the acid chloride was cooled, the crystallized mass being gradually added to 100 ml of 25% aqueous ammonia, stirred and chilled externally. Stirring was continued for 1.5 to 2 hours after the addition had been completed. The amide was filtered out and crystallized from butyl alcohol. The yield was 16.9 g (85% of the theoretical). Extremely minute white needles with an m.p. of 233-235°, slightly soluble in water and crystallizable from 1:60 ethyl alcohol and from 1:40 butyl alcohol.

4.855 mg substance: 9.07 ml 0.01 N H_2SO_4. 4.833 mg substance: 8.99 ml 0.01 N H_2SO_4.
Found %: N 26.15, 26.04. $C_{11}H_{15}O_3N_5$. Calculated %: N 26.41.

b) 4.5 grams of the methyl ester of caffeine propionic acid was agitated in a stoppered bottle for 24 hours with 60 ml of methanol and 50 ml of 28.5% aqueous ammonia. The amide was then filtered out, washed with water, and dried. M.p. 232-234°; weight 2.4 g (52% of the theoretical). After the mother liquor had been evaporated in vacuo and acidulated, we recovered 1.4 g of caffeine propionic acid, equivalent to 34% of the theoretical.

Dimethylamide of β-(caffeine-8)-propionic acid. 3-4 ml of liquid dimethylamine was poured into a chilled solution of 5 g of unrefined caffeinepropionyl chloride in 50 ml of absolute benzene. The reaction mixture was set aside to stand in a stoppered bottle at room temperature. The crystalline dimethylamide with an m.p. of 186-188°, gradually settled out of the transparent solution. The yield was 2.6 g (50% of the theoretical). Snow-white needles with an m.p. of 188-189°, soluble in the cold in chloroform, and crystallizable from 1:1 water, from 1:20 alcohol, from 1:30 ethyl acetate, and from 1:50 benzene.

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*) The thionyl chloride was refined by boiling it with sulfur, followed by fractional distillation [7].

5.846 mg substance: 10.01 ml 0.01 N H_2SO_4. 6.016 mg substance: 10.42 ml 0.01 N H_2SO_4.
Found %: N 23.97, 24.25. $C_{13}H_{19}O_3N_5$. Calculated %: N 23.88.

Dimethylaminoethyl ester of β-(caffeine-8)-propionic acid (hydrochloride). A cold solution of 3 g of unrefined caffeinepropionyl chloride in benzene was stirred at room temperature while 1.1 g of redistilled dimethylaminoethanol was added. The reaction mass was then stirred for 3 hours at the boiling point of benzene. The reaction mass was cooled, and the precipitated hydrochloride of the dimethylaminoethyl ester of caffeinepropionic acid was filtered out and recrystallized from butyl alcohol. The yield was 2.8 g (71% of the theoretical). Minute white needles with an m.p. of 222-224°, freely soluble in water, insoluble in benzene, crystallizable from ethyl alcohol and butyl alcohol.

7.719 mg substance: 2.955 mg AgCl. 6.759 mg substance: 2.555 mg AgCl.
Found %: Cl 9.47, 9.35. $C_{15}H_{23}O_4N_5 \cdot HCl$. Calculated %: Cl 9.54.

Diethylaminoethyl ester of β-(caffeine-8)-propionic acid (hydrochloride). A cold solution of 3 g of unrefined caffeinepropionyl chloride in benzene was stirred while 1.23 g of redistilled diethylaminoethanol was gradually added. The reaction mass was then stirred for 3.5 hours at the boiling point of benzene. The precipitated hydrochloride of the diethylaminoethyl ester of caffeinepropionic acid was filtered out and crystallized from butyl alcohol. The yield was 1.5 g (36% of the theoretical). Minute white needles with a m.p. of 226-228°, freely soluble in water, insoluble in benzene, and crystallizable from ethyl and butyl alcohol.

6.765 mg substance: 2.439 mg AgCl. 6.603 mg substance: 2.346 mg AgCl.
Found %: Cl 8.92, 8.79. $C_{17}H_{27}O_4N_5 \cdot HCl$. Calculated %: Cl 8.84.

SUMMARY

1. A method has been found for synthesizing caffeine derivatives with aliphatic acid groups containing a three-membered carbon chain at the 8-position from caffeine-8-aldehyde.

2. It has been found that the caffeine derivatives with mono- and dibasic aliphatic acid groups containing a three-membered carbon chain substituted at the 8 position are highly stable, in contrast to the highly unstable 8-caffeinecarboxylic acid and caffeinacetic acids.

3. The following acids have been synthesized: (caffeine-8)-methylenemalonic acid, (caffeine-8)-isosuccinic acid, β-(caffeine-8)-acrylic acid, and β-(caffeine-8)-propionic acid, as well as their methyl and ethyl esters. We have also synthesized the dimethylaminoethyl and diethylaminoethyl esters, and the amide and dimethylamide of β-(caffeine-8)-propionic acid.

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Received March 13, 1950

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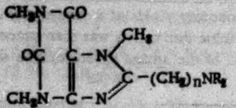
THE 8- SUBSTITUTION DERIVATIVES OF METHYLATED XANTHINES

III. AMINOMETHYL AND AMINOETHYLCAFFEINE AND THEIR ALKYLATED DERIVATIVES

E. S. Golovchinskaya and E. S. Chaman

In our continuation of the research initiated [1] on the synthesis of 8-substitution derivatives of methylated xanthines the problem arose of investigating 8-aminomethylcaffeine, 8-aminoethylcaffeine, and their alkylated derivatives.



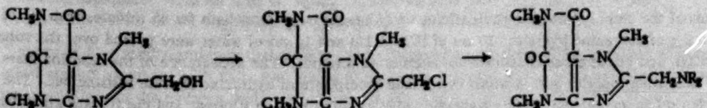
R = H, CH_3, C_2H_5; n = 1 or 2.

The method of synthesizing derivatives of methylated xanthines with amine groups substituted at the 8 position described in the literature [2] is extraordinarily complicated. The method involves the acylation of mono- or dimethylated 2,6-dihydroxy-4,5-diaminopryrimidine with monochloro aliphatic acids instead of the formic acid employed in synthesizing xanthine. The subsequent substitution of an amino or alkylamino group for the halogen and the closure of the imidazole ring by an alkali result in the formation of an xanthine derivative that is methylated in the pyrimidine portion of the molecule, with an aliphatic amine or alkylamine substituted at the 8 position. For example, acylating the diamine of chloracetic acid and substituting an amino group for the chlorine, followed by ring closure and methylating the resultant 8-substitution derivative of xanthine, ought to result in synthesis of aminomethylcaffeine or of its alkylated derivatives.

It is much simpler and cheaper to synthesize these compounds by starting out with 8-monochloromethylcaffeine and substituting amino or alkylamino groups for the active chlorine.

Reacting chloromethylcaffeine with dialkylamines results in the synthesis of dialkylamino derivatives, the yields being almost quantitative, whereas replacing the halogen by an unsubstituted amino group meets with various difficulties. This substitution was carried out in two ways: by synthesizing a phthalylamino derivative and then saponifying its hydrazine hydrate, or by means of a reaction with hexamethylenetetramine. In neither case was the yield of the amine higher than 45% of the theoretical.

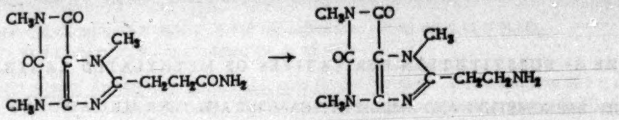
Using the 8-hydroxymethylcaffeine described in one of our previous reports [1] enabled us to eliminate the difficult operation of separating the mixture of chlorinated substances that is invariably produced when 8-methylcaffeine is chlorinated. This mixture is hydrolyzed, and the hydroxymethylcaffeine is isolated from the hydrolyzed substances by utilizing its low solubility in organic solvents. It is again produced, with a high yield of chloromethylcaffeine, when heated with thionyl chloride.



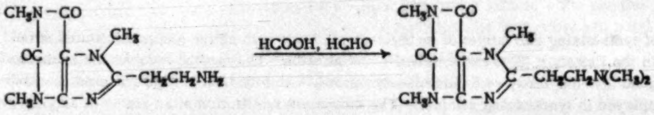
R = H, CH_3, C_2H_5

We prepared phenylaminomethylcaffeine by hydrogenating 8-caffeinylideneaniline [1] with Raney's nickel in alcohol.

With a view to synthesizing 8-aminoethylcaffeine, we investigated the feasibility of converting the β-caffeinepropionamide described in our preceding report [3] into caffeinethylamine in a Hofmann reaction.



This reaction was not impeded by the fact that the initial amide is nearly insoluble in water, since the resultant chloramide or bromamide of caffeinepropionic acid is soluble enough. This made it possible to effect 100 % conversion into an aqueous solution in a comparatively short time when the hypochlorite or hypobromite was reacted with the amide at 2 - 3°. Nor did the high sensitivity of the caffeine ring to alkalies, which is particularly great during heating, interfere with the successful carrying out of the reaction. We were able to convert the bromide into an amine within 5-7 minutes, i.e., within an interval in which most of the substance is not broken down by the alkali, notwithstanding the fairly high reaction temperature (60-70°). These conditions enable us to secure fairly satisfactory yields of 8-aminoethylcaffeine (44-52% of the theoretical, based on the original amide). This caffeine derivative was then successfully converted into dimethylaminoethylcaffeine by methyating a solution of the amine hydrochloride with a mixture of formaldehyde and formic acid.



We are sincerely grateful to O. Yu. Magidson for his assistance in this research.

EXPERIMENTAL

8-Chloromethylcaffeine. 50 grams of 8-hydroxymethylcaffeine was heated on a water bath for 6 hours with 135 ml of thionyl chloride. The resultant transparent solution crystallized during the reaction. After the solution had cooled, the crystals were suction-filtered out, washed with ether, and dried. They weighed 42.8 g; m. p. 215.5-216°. The thionyl chloride was driven off from the filtrate, the 10 g of residue being crystallized from ethyl acetate. The crystals weighed 6 g, m.p. 214.5-215.5°. The total yield of 8-chloromethylcaffeine was 48.8 g, or 90% of the theoretical.

8-Aminomethylcaffeine. 1) 2.4 grams of potassium phthalimide was added to a boiling solution of 2.4 g of 8-chloromethyl caffeine in 20 ml of chlorotoluene. After 5 hours of heating the chlorotoluene was driven off, its residual traces being driven off with steam. The aqueous suspension was hot-filtered, the resultant 8-phthalylaminomethylcaffeine being crystallized from 40 ml of toluene. It weighed 1.6 g, m.p. 247.5-248.5°.

0.1841 g substance; 25.89 ml 0.1 N H_2SO_4. 0.2180 g substance; 30.51 ml 0.1 N H_2SO_4.
Found %: N 19.68, 19.59. $C_{17}H_{15}O_4N_5$. Calculated %: N 19.83.

1.6 grams of the phthalylaminomethylcaffeine was heated on a water bath for 45 minutes with 10 ml of alcohol and 0.6 g of hydrazine hydrate. 10 ml of HCl (1.19) and 10 ml of water were poured over the voluminous, swollen mass, and heating was continued for another 45 minutes. The appearance of the reaction mass changed again, becoming mobile, with a small crystalline precipitate of hydrazine hydrate settling out. The alcohol was driven off in vacuo, the phthalylhydrazide (1.3 g) being suction filtered, and the filtrate alkalinized and repeatedly extracted with chloroform. The extracts were dried with calcined Na_2SO_4 and the chloroform driven off, yielding a residue that weighed 1.5 g. It was crystallized from 150 ml of toluene. Thin pliant needles with an m.p. of 203-205°. The yield was 1 g, or 45% of the theoretical.

0.0940 g substance: 20.92 ml 0.1 N H_2SO_4. 0.1065 g substance: 23.72 ml 0.1 N H_2SO_4.
Found %: N 31.15, 31.19. $C_9H_{13}O_2N_5$. Calculated %: N 31.39.

2) A solution of 1.4 g of 8-chloromethylcaffeine and 0.7 g of hexamethyltetramine in 45 ml $CHCl_3$ was heated on a water bath for 2.5 hours. The transparent solution soon turned cloudy as a voluminous white precipitate began to settle out. Upon cooling the reaction mass was filtered, the crystalline salt being air-dried. It weighed 1.3 g. The resultant salt was heated for 20 minutes with 4.8 ml of a 10% solution of HCl in 95% ethyl alcohol, after which the alcohol was driven off. It was reheated with 1.6 ml of the same alcohol, and the mixture of the alcohol with the resultant acetal was again driven off. This last operation was repeated two more times. The flask residue was treated with a bicarbonate solution and repeatedly extracted with chloroform. The extract was dried, and the chloroform driven off. The residue weighed 0.55 g, or 40% of the theoretical. M.p. 201-203°. The m.p. was raised to 203-205° after crystallization from toluene or amyl alcohol. The substance was the same as that produced in the preceding reaction, the mixed melting point being 203-205°.

1 gram of 8-aminomethylcaffeine was dissolved in 3 ml of HCl (1.19), and absolute ethyl alcohol saturated with HCl was added to the solution. The precipitated hydrochloride, with an m.p. of 280-282°, was suction-filtered and twice crystallized from 30 times its weight of 80% ethyl alcohol. Minute white needles, excellently soluble in water, with an m.p. of 284-286°.

6.106 mg substance: 3.345 mg AgCl. 6.894 mg substance: 3.837 mg AgCl.
Found %: Cl 13.55, 13.76. $C_9H_{13}O_2N_5 \cdot HCl$. Calculated %: Cl 13.68.

8-Diethylaminomethylcaffeine. 15 grams of 8-chloromethylcaffeine was boiled on a water bath for 4 hours with 150 ml of diethylamine. The appearance of the reaction mass changed from a thick paste to a mobile transparent solution with transparent crystals suspended in it. The excess diethylamine was driven off, and the residue treated with water. The substance filtered out of the solution of the diethylamine hydrochloride weighed 17.1 g, or 99.7% of the theoretical; m.p. 110°. It crystallized from water in very thin minute needles, and from ether as snow-white, thin, elongated, orthogonal lamellae; m.p. 111.5-113°

5.384 mg substance: 9.53 ml 0.01 N H_2SO_4. 6.231 mg substance: 11.10 ml 0.01 N H_2SO_4.
Found %: N 24.79, 24.96. $C_{13}H_{21}O_2N_5$. Calculated %: N 25.08.

A 15% solution of HCl in absolute ethyl alcohol was added to an ether solution of 8-diethylaminomethylcaffeine until its reaction with Congo red was faintly acid. The hydrochloride settled out as an oil that gradually crystallized. It was recrystallized from 10 times its weight of 96% alcohol. Quadrangular, transparent, white lamellae, m.p. 236 (with decomp.).

6.525 mg substance: 3.130 mg AgCl. 5.025 mg substance: 2.315 mg AgCl.
Found %: Cl 11.44, 11.40. $C_{13}H_{21}O_2N_5 \cdot HCl$. Calculated %: Cl 11.22.

8-Dimethylaminomethylcaffeine. 7.5 grams of chloromethylcaffein was heated to 50-60° for a long time in a sealed tube with 50 ml of dimethylamine, with frequent shaking.

After dissolution was complete, the excess dimethylamine was driven off, the residue dissolved in water, and the base isolated by adding 40% NaOH, the flask being cooled externally. The base separated out as an oil that solidified quickly; then it was suction-filtered out and dissolved in chloroform. The solution was dried over calcined Na_2SO_4, and the chloroform driven off, the residue weighing 7.5 g, or 95.5% of the theoretical. M.p. 124-125°. It crystallized from ether as elongated transparent lamellae. M.p. of the recrystallized substance: 125-126°.

4.402 mg substance: 8.70 ml 0.01 N H_2SO_4. 4.246 mg substance: 8.33 ml 0.01 N H_2SO_4.
Found %: N 27.67, 27.47. $C_{11}H_{17}O_2N_5$. Calculated %: N 27.88.

7 grams of 8-dimethylaminomethylcaffeine was dissolved by gentle heating in 60 ml of ethyl alcohol, and 20 ml of alcohol saturated with HCl was added to make the reaction with Congo red slightly acid. A crystalline precipitate of the hydrochloride settled out. It weighed 7.7 g; m.p. 266-267°. It was recrystallized from 150 ml of 80% alcohol. Needles with an m.p. of 269-271°.

5.271 mg substance: 9.1 ml 0.01 N H_2SO_4. 5.207 mg substance: 8.98 ml 0.01 N H_2SO_4.
8.110 mg substance: 4.070 mg AgCl. 7.285 mg substance: 3.702 mg AgCl.
Found %: N 24.25, 24.14; Cl 12.42, 12.57. $C_{11}H_{17}O_2N_5 \cdot HCl$. Calculated %: N 24.34 Cl 12.34.

8-Phenylaminomethylcaffeine. A suspension of 5 g of 8-caffeinylideneaniline [1] in 200 ml of ethyl alcohol was hydrogenated with 2.5 g of Raney's nickel at room temperature, with mechanical stirring, 440 ml of hydrogen being absorbed within 3.5 hours. The decolorized suspension was heated with 200 ml of alcohol until all the precipitate dissolved, after which the solution was filtered. When the filtrate cooled, 4 g of phenylaminomethylcaffeine, with an m.p. of 190-192°, settled out. Driving off the alcohol and crystallizing the residue yielded another 0.3 g of the amine. The yield totaled 4.3 g, or 86% of the theoretical. The substance dissolves 1:1200 in hot water and 1:70 in alcohol. Minute white needles with an m.p. of 193-194°. It forms readily hydrolyzable salts.

5.723 mg substance: 9.52 ml 0.01 N H_2SO_4. 6.305 mg substance: 10.46 ml 0.01 N H_2SO_4.
Found %: N 23.29, 23.11. $C_{15}H_{17}O_2N_5$. Calculated %: N 23.41.

8-Aminoethylcaffeine. A chilled solution of sodium hypobromite, prepared from 9 g of bromine and 56.3 ml of a 10% NaOH solution, was added drop by drop during the course of an hour, at 35° and with constant stirring, to a suspension of 14 g of caffeinepropionylamide in 100 ml of water. The amide gradually dissolved, the solution being stirred for another 50-60 minutes at 3-5°, after which 60 ml of a 10% NaOH solution was added. Then the reaction mass was heated to 60° for 20-25 minutes and stirred for another 10 minutes at 60-70°. The reaction was considered to be complete when no bromine was liberated from a sample that was acidified with hydrochloric acid. Then the solution was quickly cooled to 20-25° and poured into 100 ml of HCl (1.19), causing the active evolution of CO_2. The acid solution was concentrated in vacuo to a volume of 30-40 ml, the crystallizing sodium chloride filtered out, and the filtrate evaporated in vacuo to dryness. The residue was chilled with ice and treated with a 26% NaOH solution in chloroform the separating aqueous solution being extracted again with chloroform. The chloroform solution was dried over Na_2SO_4 and the chloroform driven off. The residue (6.8 g) was dissolved in 30-35 ml of 96% ethyl alcohol, and an alcoholic solution of HCl was added until the reaction with Congo red was slightly acid. A white crystalline precipitate of the hydrochloride gradually settled out; it was recrystallized from 80% ethyl alcohol. The yield was 6.3 g (44.1% of the theoretical).

8-Aminoethylcaffeine hydrochloride is very soluble in water and crystallizes from 80% ethyl alcohol and from butyl alcohol. White needles with an m.p. of 348-350° (decomp.).

7.158 mg substance: 3.829 mg AgCl. 7.161 mg substance: 3.787 mg AgCl. 5.015 mg substance: 9.13 ml 0.01 N H_2SO_4. 5.095 mg substance: 9.20 ml 0.01 N H_2SO_4. Found %: N 25.49, 25.28; Cl 13.23. 13.08. $C_{10}H_{15}O_2N_5 \cdot HCl$. Calculated %: N 25.59; Cl 12.98.

The base was isolated, as described above, from an aqueous solution of the purified hydrochloride by a 26% alkali solution. The base was refined by recrystallization from toluene.

The 8-aminoethylcaffeine base is freely soluble in water, chloroform, alcohol, ethyl acetate, and acetone, and slightly soluble in benzene. Yellowish needles with an m.p. of 143-144°.

4.397 mg substance: 9.17 ml 0.01 N H_2SO_4. 4.196 mg substance: 8.76 ml 0.01 N H_2SO_4.
Found %: N 29.17, 29.23. $C_{10}H_{15}O_2N_5$. Calculated %: N 29.53.

8-Benzylideneaminoethylcaffeine. 0.5 gram of benzaldehyde was added to a solution of 1 g of 8-aminoethylcaffeine in alcohol. The mixture was heated for 20 minutes, the yellowish needles of the benzylidene base crystallizing out upon cooling. The yield was 0.8 g (61.5% of the theoretical). The substance crystallizes from methanol and ethyl alcohol. It is hydrolyzed when heated with water. White needles with an m.p. of 180-181°.

4.749 mg substance: 7.32 ml 0.01 N H_2SO_4. 4.623 mg substance: 7.14 ml 0.01 N H_2SO_4.
Found %: N 21.58, 21.61. $C_{17}H_{19}O_2N_5$. Calculated %: N 21.54.

8-Dimethylaminoethylcaffeine. A solution of 7.6 g of 8-aminoethylcaffeine hydrochloride in 15 ml of water was added a drop at a time during the course of 40-50 minutes to a methylating mixture consisting of 8 g of a 28.69% solution of formalin and 8 g of 85% formic acid, heated to 95°. After the reaction mass had been stirred for 8 hours at 100-102°, it was chilled with a snow-salt mixture. The amine was isolated by processing with a 26% alkali solution and then quickly extracting with chloroform. The chloroform solution was dried over calcined Na_2SO_4, the chloroform being driven off, and the residue crystallized from diethyl ether. The yield was 5 g, or 68.5% of the theoretical. Minute white needles with an m.p. of 100-102°. Freely soluble in the cold in water, chloroform, alcohol, and benzene and soluble when heated in diethyl ether.

3.891 mg substance: 7.266 ml 0.01 N H_2SO_4. 2.595 mg substance: 4,89 ml 0.01 N H_2SO_4.
Found %: N 26.14, 26.40. $C_{12}H_{19}O_2N_5$. Calculated %: N 26.41.

A solution of HCl in absolute alcohol was added to an ether solution of 8-dimethylaminoethylcaffeine until the reaction with Congo red was slightly acid. The finely crystalline white precipitate of the hydrochloride was recrystallized from 96% alcohol. Minute white needles, freely soluble in water, decomposing at 257°.

5.975 mg substance: 2.829 mg AgCl. 7.136 mg substance: 3.420 mg AgCl.
Found %: Cl 11.71, 11.85. $C_{12}H_{19}O_2N_5 \cdot HCl$. Calculated %: Cl 11.77.

SUMMARY

1. A method is set forth for synthesizing 8-aminomethylcaffeine and its alkylated derivatives from 8-chloromethylcaffeine.

2. The conditions required for converting β-(caffeine-8)-propionamide into 8-aminoethylcaffeine have been determined.

3. The following compounds have been synthesized: 8-aminomethylcaffeine, 8-dimethylaminomethylcaffeine, 8-diethylaminomethylcaffeine, 8-aminoethylcaffeine, 8-dimethylaminoethylcaffeine, and the hydrochlorides of these compounds, as well as 8-phenylaminomethylcaffeine, and 8-benzylideneaminoethylcaffeine.

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Received March 13, 1950.

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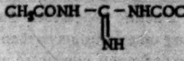
*) See Consultants Bureau English translation, p. 593.

THE TRANSFORMATION OF GUANIDINE DURING ACETYLATION[1]

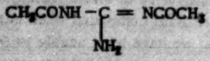
A. A. Ryabinin

When Korndorfer acetylated the salts of guanidine [1], he secured compounds that he described as symmetric (I) and asymmetric (II) diacetylguanidines and the anhydride of diacetylguandine (III).



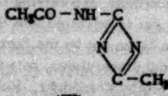
$$CH_3CONH-\overset{}{\underset{\underset{NH}{\|}}{C}}-NHCOCH_3$$

(I)



$$CH_3CONH-\underset{\underset{NH_2}{|}}{C}=NCOCH_3$$

(II)



(III)

Although a large number of substituted guanidines has been synthesized by now, no one has succeeded in isolating tautomers resembling (I) and (II). We were, therefore, interested in checking Korndorfer's research. We secured a substance, $C_5H_9O_2N_3$, with an m.p. of 166°, by heating salts of guanidine to 100° with twice their weight of acetic anhydride. The formula for this compound is that for diacetylguanidine as well as for an acetate of the anhydride of monoacetylguanidine like (III), for example. Analysis of the picrate of the $C_5H_9O_2N_3$ substance indicated that it was the monopictrate of diacetylquanidine. Thus, the $C_5H_9O_2N_3$ substance with an m.p. of 166° we had prepared was a diacetylguanidine hitherto unknown in the literature.

When Korndorfer acetylated guanidine carbonate under the same conditions, he secured an acetate of a monoacetyl derivative. This was because he employed recrystallization from water. Our diacetylguanidine was extremely unstable, being totally converted into monoacetylguanidine acetate when heated for a long time in alcohol.

When we heated guanidine acetate of carbonate with five times its weight of acetic anhydride to the boiling point of the solution, we secured two other substances: $C_6H_9ON_5$, with an m.p. of 285°, and $C_8H_{11}O_2N_5$, with an m.p. of 217.5°. These formulas differ by one acetyl group. We noticed that the compound $C_8H_{11}O_2N_5$ was unstable. It loses an acetyl group when recrystallized from 5% acetic acid, being converted into the other synthesized compound, $C_6H_9ON_5$. The converse transformation was effected by boiling with acetic anhydride. The elementary composition of these substances as well as the methods employed in their formation make it probable that their structure is that of acetyl derivatives: 4, 6-diamino-2-methyl-1, 3, 5-triazine (IV).

M. Nencki [2], Diels [3], and Simons and Weaver [4] have observed that 4, 6-diamino-2-methyl-1,3,5-triazine is formed when the acetate or the monoacetyl derivative of quanidine was heated to 190-230°. In our experiments, we found that the reaction proceeded under milder conditions when an excess of acetic anhydride was present.

A. Ostrogovich [5] secured 4, 6-diacetylamino-2-methyl-1, 3, 5-triazine (V) with an m.p. of 212-213° by acetylating 4, 6-diamino-2-methyl-1, 3, 5-triazine, while recrystallizing the compound (V) from ethyl acetate or acetic acid yielded 4-amino-6-acetylamino-2-methyl-1, 3, 5-triazine with an m.p. of 284° (VI). It is obvious that these compounds are the same as those we synthesized.

The slight discrepancy in the melting points of the diacetyl derivative is due to the ease with which this compound is decomposed.

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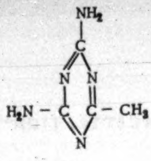
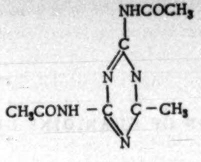
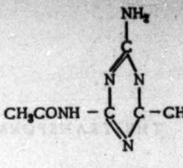
[1] The contents of a research paper by Grundmann and Beyer recently published (Ber. 83, 452) are very close to those of the present paper. Where the two papers agree, they reach the same conclusions. The paper of the foregoing authors was submitted to the editors on March 31, 1950, i.e., at practically the same time as the present paper reached the editors of the Journal of General Chemistry of the U.S.S.R.



(IV)



(V)



(VI)

There is no doubt that the anhydride of diacetylguanidine, with an m.p. of 210-212°, and the asymmetric diacetylguanidine, with an m.p. of 271°, described by Korndorfer, are the impure di- and monoacetyl derivatives of 4, 6-diamino-2-methyl-1, 3, 5-triazine. This is shown by a comparison of their melting points and the reciprocal transformations of the substance synthesized by Korndorfer and by us. In Korndorfer's experiments, for example, saponifying the anhydride of diacetylguanidine yielded asymmetrical diacetylguanidine, which was reconverted into the original compound when heated with acetic anhydride. Our conclusion is likewise borne out by the fact that we have been unable to secure any other substances than those described above and diacetylurea, notwithstanding our numerous acetylation experiments conducted under the conditions described by Korndorfer. Korndorfer's symmetric diacetylguanidine, with an m.p. of 152°, which forms no salts, is apparently identical with the diacetylurea. The mistake made by that author lay in his failure to make a nitrogen determination.

EXPERIMENTAL

Preparation of guanidine acetate. 50 grams of guanidine carbonate was dissolved in water, neutralized with acetic acid, and evaporated to dryness in vacuo. The acetate was crystallized from alcohol as prisms with an m.p. of 229° by adding ether (the m.p. is given as 229-230° in the literature [6]).

Preparation and analysis of diacetylguanidine. In one of our runs 5 g of guanidine acetate was heated on a boiling water bath for two hours with 10 g of acetic anhydride (b.p. 137-139°). Two grams of crystals, in the shape of large needles, settled out of the cooled solution. The substance had a melting point of 166° after having been dried at 95°. The melting point did not change after rapid recrystallization from 95% alcohol and drying.

0.1175 g substance: 0.1800 g CO_2; 0.0676 g H_2O. 0.1169 g substance: 0.1778 g CO_2; 0.0687 g H_2O. 0.0731 g substance: 19.10 ml N_2 (22°, 760 mm). Found %: C 41.78, 41.48; H 6.44, 6.57; N 29.44. $C_5H_9O_2N_3$. Calculated %: C 41.93; H 6.34; N 29.37.

Preparation and analysis of diacetylguanidine picrate. 0.3 gram of diacetylguanidine and 0.48 g of picric acid were dissolved in separate portions of methanol. When the two solutions were combined, a finely crystalline picrate, with an m.p. of 163-164°, settled out. Recrystallization from absolute methanol yielded the picrate as large yellow needles with an m.p. of 164-165°.

0.0596 g substance: 12.02 ml N_2 (23°, 764 mm). Found %: N 22.74. $C_5H_9N_3O_2 \cdot C_6H_3N_3O_7$. Calculated %: N 22.59.

Preparation and analysis of monoacetylguanidine acetate. 5 grams of guanidine acetate was heated on a boiling water bath for two hours with 10 g of acetic anhydride. The crystals that settled out as the solution cooled were filtered out and twice recrystallized from 95% alcohol without having been dried. This yielded 2 g of needles with an m.p. of 177-178° (the m.p. given in the literature is 177-178° [1]). The mixed melting point with diacetylguanidine was 150°.

0.1233 g substance: 0.1699 g CO_2, 0.0805 g H_2O. 0.1266 g substance: 0.1730 g CO_2; 0.0804 g H_2O. 0.0708 g substance: 16.30 ml N_2 (22°, 768 mm). Found %: C 37.58, 37.27; H 7.30, 7.10; N 26.22. $C_5H_{11}O_3N_3$. Calculated %: C 37.24; H 6.88; N 26.08.

Preparation of monoacetylguanidine picrate. This salt was prepared as described above; the minute yellow needles melted at 237.5-238.5°.

Preparation and analysis of 4,6-diacetylamino-2-methyl-1, 3, 5-triazine. 1 gram of guanidine acetate was boiled for one hour with five g of acetic anhydride. The crystals that settled out upon cooling were dried in vacuo over alkali. The substance had a m.p. of 217.5° after double recrystallization from boiling water. 5.3 grams of the same substance was secured from 15 g of guanidine carbonate by a similar procedure.

0.1230 g substance: 0.2077 g CO_2; 0.0590 g H_2O. 0.1118 g substance: 0.1875 g CO_2; 0.0540 g H_2O. 0.0651 g substance: 19.45 ml N_2 (22°, 760 mm). Found %: C 46.05, 45.74; H 5.37, 5.40; N 33.66. $C_8H_{11}O_2N_5$. Calculated %: C 45.69; H 5.28; N-33.34.

Preparation and analysis of 4-amino-6-acetylamino-2-methyl-1, 3, 5-triazine. 5 grams of guanidine acetate was boiled for one hour with 25 g of acetic anhydride. The resulting crystals were recrystallized from boiling water without having been dried. This yielded 1.35 g of crystals with an m.p. of 284°. The m.p. rose to 285° after four recrystallizations from boiling water.

0.1209 g substance; 0.1900 g CO_2; 0.0596 g H_2O. 0.1152 g substance: 0.1819 g CO_2; 0.0580 g H_2O. 0.0410 g substance: 14.98 ml N_2 (22°, 769 mm). Found %: C 42.86, 43.06; H 5.52, 5.63; N 41.67. $C_6H_9ON_5$. Calculated %: C 43.09; H 5.43; N 41.91.

Preparation and analysis of diacetylurea. The mother liquors secured in the preceding experiments after the crystalline substances that settled out of the acetic anhydride had been filtered out were concentrated in vacuo. The resulting crystalline deposits constituted a mixture that fused broadly in the 130-145° range. The deposits were combined and fractionated by recrystallization from alcohol. This yielded, in addition to the substances secured in the previous tests, 2 g of pure diacetylurea, with an m.p. of 154.5 - 155.5° (the m.p. is given in the literature as 152-153° [6]. The mixed melting point with diacetylguanidine was unsharp, beginning at 124°.

0.1136 g substance: 0.1728 g CO_2; 0.0556 g H_2O. 0.0516 g substance: 8.70 ml N_2 (20°, 770 mm). Found %: C 41.49; H 5.48; N 19.44. $C_5H_8O_3N_2$. Calculated %: C 41.64; H 5.59; N 19.44.

Conversion of diacetylguanidine into monoacetylguanidine acetate. A few grams of diacetylguanidine, with an m.p. of 166°, was recrystallized from 95% alcohol. After the first recrystallization the melting point dropped to 164-165°, while after the second we secured a substance with an m.p. of 178°. The mixed melting point with monoacetylguanidine acetate exhibited no depression.

Conversion of monoacetylguanidine acetate into 4, 6-diacetylamino-2-methyl-1, 3, 5-triazine. One gram of monoacetylguanidine was boiled for one hour with 5 g of acetic anhydride. When the solution cooled, crystals with an m.p. of 214° settled out. The mixed melting point with the pure substance was 216°.

Reciprocal conversions of 4, 6-diacetylamino-2-methyl-1, 3, 5-triazine and 4-amino-6-acetylamino-2-methyl-1, 3, 5-triazine. A few grams of 4, 6-diacetylamino-2-methyl-1, 3, 5-triazine, with an m.p. of 217°, was recrystallized from boiling 5% acetic acid. This yielded crystals with an m.p. of 285°. 0.5 gram of the resulting substance was heated with acetic anhydride. Upon cooling, crystals with an m.p. of 217° settled out.

SUMMARY

1. Diacetylguanidine, with an m.p. of 166°, and its monopicrate, which are unknown in the literature, are described.

2. It has been found that heating guanidine salts with acetic anhydride yields 4, 6-diacetylamino-2-methyl-1, 3, 5-triazine and 4-amino-6-acetylamino-2-methyl-1, 3, 5-triazine.

3. It has been shown that the two diacetyl derivatives of guanidine described in the literature — the symmetric with an m.p. of 152° and the asymmetric with an m.p. of 271° — do not exist. These names were employed erroneously to describe diacetylurea and impure 4, 6-amino-6-acetylamino-2-methyl-1, 3, 5-triazine.

4. It has been shown that the anhydride of diacetylguanidine, with an m.p. of 210-212°, described in the literature does not exist. This name was employed erroneously to describe impure 4, 6-diacetylamino-2-methyl-1, 3, 5-triazine.

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Received April 18, 1950.

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THE DENDRITIC CRYSTALLIZATION OF VARIOUS SALTS FROM AQUEOUS SOLUTIONS

I. The Formation of Dendritic Crystals of NH_4Cl, KCl, and NaCl, and Their Modification by Various Impurities. page 461.

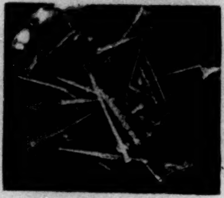
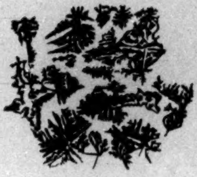


Figure 5.



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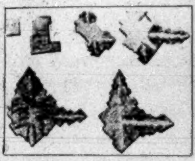

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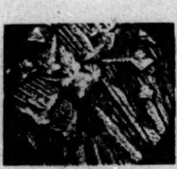

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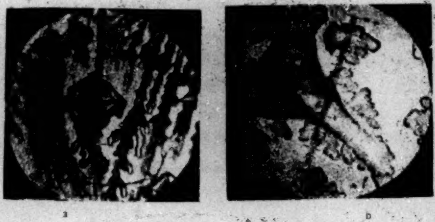

Figure 3.

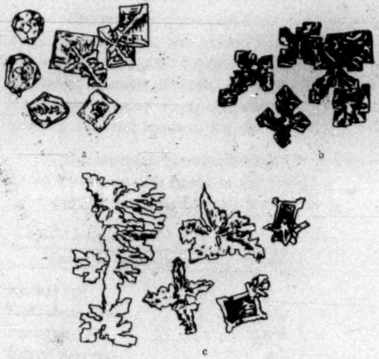

Figure 4.

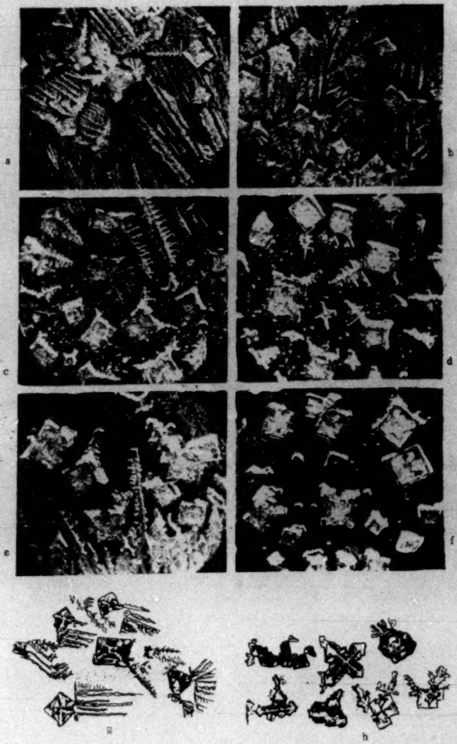

Figure 6.

THE CHEMICAL HETERODYNAMICITY OF NASCENT HYDROGEN. II.

A. K. Dmitriev

In my first report [1], I set forth the following conclusions: a) the chemical activity of nascent hydrogen varies widely, depending upon the nature of the metal at whose surface the hydrogen is evolved when the metal is dissolved in acid; and b) there is a periodicity in the change of hydrogen's chemical activity.

Although these conclusions were based upon experimental findings, these findings were not very diversified, as the substances subjected to hydrogen reduction were confined to sulfur and its compounds. Further research, therefore, required the extension of this group of substances to compounds of different composition and structure.

Increasing the number and diversity of substances suitable for this objective entailed considerable difficulty, inasmuch as their selection involved various restrictions: nonvolatility, not decomposing at 100°, feasibility of a quantitative control of the reduction process, feasibility of reduction with hydrogen but not with metals, which involved the necessity of choosing compounds with covalent bonds, and so forth. That is why it proved advisable to confine our choice to organic compounds possessing a bright color, the following being selected from the long list of such compounds: methyl red, methylene blue, pyronine, and indigo carmine.

The principal advantage of colored substances is that many of them are decolorized when reduced, thus serving as their own indicators of the end of reduction; this is extremely convenient, since the change of color during reduction is easily followed, eliminating the tedious determination of the reduction products.

Our choice of the four specified colored substances was dictated by considerations of diversity of composition and structure and by the differences in their chromophore groups.

Another objective of the present research has been a study of metallic alloys; this is of practical and theoretical interest, as may be seen from what follows.

EXPERIMENTAL

The series of reduction tests was run as follows: a standard volume of a solution of an organic compound, of given concentration, was poured into a beaker, a certain volume of 1:1 hydrochloric acid was added, and the solution was heated to a gentle boil on an electric hot plate, after which the metal was added in powder form to the solution gradually, in small portions, until the colored solution was decolorized as the result of reduction by hydrogen. Then the residual unused metal was weighed, the difference between this weight and that of the original sample giving the quantity of metal required for the reduction of the organic compound by nascent hydrogen.

Our research has established that these tests were fully reproducible and that very different amounts of different metals were required to decolorize a given volume of solution of the colored substance, thus confirming our basic conclusions regarding the far-reaching chemical heterodynamicity of nascent hydrogen.

TABLE 1

Reduced substance	Mg	Zn	Al	Mn	Cd	Fe	Co	Ni
Methyl red	6	11	90	54	360	250	410	875
Methylene blue	3.5	13	138	100	190	225	300	465
Pyronine	2.5	10	58	50	–	60	230	300
Indigo carmine	2.5	10	70	45	–	50	150	300
KCNS	2	30	50	54	80	125	400	750

In Table 1 we give the results of four series of tests, expressed not in weights of the various metals, but recalculated and expressed in milliliters of the volume of colored solutions that can be decolorized by the dissolution of 1/24th gram-equivalent of each metal. It is obvious that the greater the volume of solution decolorized, the more active the hydrogen.

The last line gives, by way of comparison, the indexes of hydrogen activity secured in a reaction with KCNS, as stated in our first report.

Methyl red is only very slightly soluble, so that we used a saturated solution in the tests. The concentration was higher for the other dyes: 1.8 g liter for methylene blue, 1.5 g for pyronine, and 1 g for indigo carmine.

Reduction was very smooth, the color of the solution gradually growing paler until it vanished completely, except in the case of indigo carmine, the solution of which changed from dark blue to slightly greenish, which corresponds to a leuco compound, according to the literature, though other shades were sometimes visible.

In regarding the figures listed in Table 1 as a singly-valued index of the chemical activity of the hydrogen liberated at the surface of a given metal, we must first remember that here, again, as in the reduction of sulfur derivatives, the activity indexes cover a very wide range, and that the metals follow nearly the same order in point of hydrogen activity, as may be seen from inspection of the last line with those above it. In every case Mg and Zn, on the one hand, and Co and Ni, on the other, are the extremes in the metal series, when arranged in order of increasing hydrogen activity.

In reducing the organic compounds we rechecked the influence of the degree of acidity upon the reduction process and determined the influence of alkalinity upon the process. The results of our study of this problem are given in Table 2.

TABLE 2

No.	Substance reduced	Normality of HCl	Zn, weight	Normality of NaOH	AlNi, weight
1	Methyl red	4	1.97	0.8	0.37
2		3	1.3	0.4	0.32
3		2	0.8	0.2	0.3
4		1	0.6	0.1	0.28

The data cited (Table 2) show that the lower the acidity or the alkalinity, the smaller the weight of metal required for reduction, and, hence, the closer the reaction solution approaches the neutral, the better the reduction by nascent hydrogen.

We also made a study of the behavior of some alloys, mostly prepared with aluminum as a base, in order to be able to perform reduction in either an alkaline or an acid medium. These alloys contained up to 10% of the second component. The second components included those that were acid-soluble, such as Co and Ni, and the acid-insoluble ones, such as Cu, Ag, Sb and Ta. We also prepared alloys based on zinc and containing 6% of cadmium.

TABLE 3

No.	Substance reduced	Al	AlAg	AlNi	AlCu	AlCo	AlTa	AlSb	Zn	ZnCd
1	Methyl red + HCl	0.19	1.9	0.1	0.35	–	–	0.2	1.0	0.17
2	Methylene blue + HCl	0.12	0.4	0.1	0.22	–	0.12	0.13	1.5	0.43
3	Methyl red + NaOH	0.2	0.34	0.05	0.3	0.1	0.18	0.2	–	–
4	$KMnO_4$ + NaOH	0.18	0.28	0.06	0.2	0.08	0.14	0.2	–	–

We explored the behavior of these alloys in reducing methyl red and methylene blue in an acid medium and in reducing methyl red and $KMnO_4$ in an alkaline medium, using the experimental procedure outlined above. In Table 3, which gives the test results, all the numerical values represent the grams of alloy required for reducing a standard volume of a solution of the substance to be reduced. These weights identify the alloys completely: the lower the weight, the more active the hydrogen displaced from the acid or the alkali.

In these tests the following quantities were used: 450 ml of a saturated solution of methyl red + 50 ml of HCl (1:1); 450 ml of a methylene blue solution with a concentration of 1.8 g per liter + 50 ml of HCl (1:1); 30 ml of a saturated solution of methyl red + 10 ml of a 2N NaOH solution; and 200 ml of a 0.001N $KMnO_4$ solution + 40 ml of a 2N NaOH solution.

Inspection of the table shows that Cu and Ag lower the hydrogen activity in every case, this being particularly true of Ag. Decolorizing a methyl red solution in an acid medium requires 0.19 g of aluminum, but 1.8 g, or 10 times as much, of the aluminum-silver alloy.

Similar instances have been reported in electrochemistry [2]. When even small traces of Cu, Ag, or Pt are added to a metallic cathode at which reduction takes place satisfactorily, the cathode's reducing ability drops almost to zero.

In contrast to Cu and Ag, such metals as Co and, especially, Ni activate hydrogen, as might have been expected from the data in Table 1. The third series of tests in Table 3 shows that 0.2 g of Al but only 0.05 g of its alloy with Ni is required for the reduction of methyl red in an alkaline medium, i.e., the activity of the hydrogen is increased fourfold, which is not without interest for chemical practice.

Thus, the hydrogen evolved at the surface of the nobler component of an alloy is transformed by contact action, the activity of the hydrogen being raised or lowered, according to our findings, as much as tenfold in one direction and fourfold in the other in aluminum alloys.

In our subsequent more detailed research into the effect of the second component upon hydrogen activity, we found it advisable to replace alloys, which were fairly hard to prepare at times, since the melting points of some components are as high as 3000°, by deposits of one metal upon the other by means of displacing the first metal from a solution of its salt, thus achieving the same goal as in alloys: the intimate contact between the two metals. This is effected technically as follows: 1 ml of a 1% solution of a salt of the nobler metal was poured into a flask containing powdered Zn or Al, and then the solution was slightly acidulated and agitated, after which it was removed and replaced by a hot solution consisting of 100 ml of a saturated solution of methyl red and 100 ml of 2N hydrochloric acid. If subsequent heating did not produce complete decolorization, the amount of metal used was increased in the next run, and vice versa. This method was used to establish the influence of the following metals upon the activity of hydrogen: Ag, Au, Cd, Hg, Pb, Sb, Bi, Pt, and Pd.

Table 4 gives the results of these tests, the first column giving the amount of pure Zn and Al required for the reduction of the methyl red, for the sake of comparison, while the other columns give the weights of the same two metals in contact with another component.

TABLE 4

Zn	ZnAg	ZnAu	ZnCd	ZnHg	ZnPb	ZnSb	ZnBi	ZnPt	ZnPd
2	2.6	3.6	0.4	0.3	0.5	0.5	1.2	0.12	0.035
Al	AlAg	AlAu	AlCd	AlHg	AlPb	AlSb	AlBi	AlPt	AlPd
0.05	–	0.16	–	0.04	0.024	0.015	0.02	0.01	0.01

These findings clearly disclose the following behavior pattern: when the second component is at the left of Zn or Al in D. I. Mendeleev's periodic system of the elements, more of these two elements by weight is required to reduce methyl red, and, conversely, the greater the precedence of the group to which the second element belongs, the less of these two elements is required. This is very clearly seen in the tests run with Zn in contact with Au and Pd. In contact with Au 3.6 g of zinc is required instead of the 2 g of the pure metal, i.e., nearly twice as much, whereas only 0.035 g of Zn is needed when in contact with Pd, or 1/60th as much.

It is worthy of note that when $AuCl_3$ is added to the Zn with the Pd deposited upon it in order to deposit Au as well, the activating effect of the palladium is gradually paralyzed as more and more of the $AuCl_3$ is added, being completely paralyzed when the amount of $AuCl_3$ added is 20 times that of the $PdCl_2$; this agrees with the action of each of these metals upon hydrogen. Here, therefore, we see the antagonism of two components acting in opposite directions.

A study of the behavior of a large number of insoluble metals raises the question of whether the phenomenon of periodicity in the changes of hydrogen activity, set forth prudently in our first report, also applies to metals. This theoretical side of the problem was the second objective of our investigation of alloys and contact agents. In solving this problem it is advisable to make use of Table 2 in our first report, in which the metals are arranged according to the increasing activity of the hydrogen liberated at their surfaces in each row of D. I. Mendeleev's periodic table, and to expand it to include the insoluble metals, in view of the fact that if Ag and Au lower the activity of the hydrogen displaced from an acid by zinc, even though only slightly, this entitles us to place them in the table one group to the left, while, conversely, the increase in the activity of the hydrogen displaced by aluminum, due to additions of Pb, Sb, Bi, Pt, and Pd, justifies the latter elements being placed to the right of aluminum, i.e., in the senior groups of the table. Hence, the arrangement of the soluble metals in the table is based upon the numerical indexes of the hydrogen activity, which are indicated above the symbols for the metals. The insoluble metals are located according to whether they lower or raise the activity of the hydrogen displaced by zinc and aluminum (Table 5).

TABLE 5

Row	Group of elements									
	I	II	III	IV	V	VI	VII	VIII		
III		0.5 Mg	12 Al							
IV							35 Mn	50 Fe	80 Co	125 Ni
V		5 Zn								
VI									Pd	
VII	Ag	7 Cd		14 Sn	Sb					
VIII									Pt	
IX	Au	Hg		Pb	Bi					

As we see, the order in which the metals are arranged according to hydrogen activity is in no way different from their arrangement in D. I. Mendeleev's periodic table. Inasmuch as the number of metals investigated has nearly doubled, while we still observe no perceptible deviations from the general pattern of behavior, namely, that in each row of the table the hydrogen activity increases with the number of the group, we may conclude that the experiments described have not only confirmed the periodicity phenomenon, but have also extended it to the insoluble metals.

In the light of all that has been said about the periodic change in the activity of nascent hydrogen, such well-known facts as the high chemical activity of hydrogen in the presence of metals of Group VIII, such as Ni, Pt, and Pd, become quite understandable, and it is a matter of some regret that the phenomenon of periodicity in the catalytic action of metals upon hydrogen was not observed earlier, though reasons therefore existed, namely, that the strongest hydrogenation ctalysts were all in the same group (VIII), which could only be due to periodicity.

The phenomena of periodicity manifested in the catalytic action of metals upon hydrogen gives us grounds to suspect that the phenomenon of periodicity may obtain in other catalytic reactions affected by catalysts of similar composition, such as oxides of various metals, sulfides, various cations, and the like.

In conclusion, it should be pointed out that although the activity of nascent hydrogen may be extremely high at times, there is no reason to exaggerate it, and this hydrogen may compete as a reducing agent only in rare cases with such energetic reducers as $Sn^{\cdot\cdot}$, $Cr^{\cdot\cdot}$, $Ti^{\cdot\cdot\cdot}$, and $V^{\cdot\cdot}$, as is proved by the fact that a methyl red solution is decolorized at a moderate rate in the presence of Ni dissolving in an acid, whereas all we have to do to cause this decolorization to take place almost instantaneously is to throw a grain of chromium, tin, ferrotitanium, or ferrovanadium into the solution. Only the presence of disperse Pt or Pd renders the hydrogen active enough to compete as a reducing agent with the foregoing ions. This is allowed for in the recent literature, the reduction of nitrobenzene in the presence of Sn and HCl being attributed to $Sn^{\cdot\cdot}$ rather than to hydrogen.

V. A. Kustodina rendered great technical assistance in the completion of this section of the research.

SUMMARY

1. The differences in the chemical activity of the hydrogen evolved at various metals have been confirmed by reducing a number of new objects: methyl red, methylene blue, pyronine, indigo carmine, and permanganate, it having been found that the differences are as great as they were in the reduction of sulfur derivatives.

2. The conclusion regarding the periodicity obtaining in the change of the activity of nascent hydrogen made in our first report has been confirmed by a study of the effect of various acid-insoluble metals upon hydrogen: Ag, Au, Hg, Pb, Sb, Bi, Pt, and Pd.

3. In a study of alloys and contact agents of two metals it has been found that the second component may lower the hydrogen activity tenfold (as in Ag) or increase it 60 times (as in Pd).

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Received July 10, 1950.

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SOLUBILITY EQUILIBRIA IN THE $K_2Cr_2O_7 - K_2SO_4 - H_2O$ SYSTEM

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Research into the equilibria in the $K_2Cr_2O_7 - K_2SO_4 - H_2O$ system represents a continuation of our comparative study of the mutual solubility of salts in simple ternary aqueous systems that contain potassium as the common ion and potassium dichromate as the common salt component [1].

The findings on the mutual solubility of potassium bichromate and sulfate are of practical importance in dichromate technology, inasmuch as the aqueous system consisting of these salts is a part of the reciprocal $Na_2Cr_2O_7 + K_2SO_4 \rightleftarrows K_2Cr_2O_7 + Na_2SO_4$ system, often employed in preparing potassium dichromate from sodium dichromate. This aqueous system of salts is also produced in the conversion of a chromate into a dichromate in the reaction $2K_2CrO_4 + H_2SO_4 = K_2Cr_2O_7 + K_2SO_4 + H_2O$, which is ordinarily used in the final stage of the technological process to prepare dichromate from chrome iron ore.

In so far as we have been able to gather from the literature, the $K_2Cr_2O_7 - K_2SO_4 - H_2O$ system has not been investigated at all. We have secured experimental data for the following solubility isotherms: 20, 25, 30 and 40°, for this system by the procedures usually employed in the isothermal method.

The composition of the liquid phase was established by determining the $SO_4^{''}$ and $Cr_2O_7^{''}$ quantitatively. These determinations were used to calculate the percentages of $K_2Cr_2O_7$ and K_2SO_4 in the analyzed sample of the liquid phase. The $SO_4^{''}$ was determined gravimetrically, while the $Cr_2O_7^{''}$ was determined by iodometric titration. The experiments used to determine the given composition were repeated, as a rule. The composition at the isothermal invariant points is the mean value of numerous determinations, the results of the various analyses exhibiting good coincidence.

The composition of the solid phase in equilibrium with the solution was determined chiefly by observing the appearance of a bottom sample under the microscope. In the microscope's field the triclinic colored crystals of potassium dichromate are sharply distinct from the colorless crystals of potassium sulfate. In monovariant isothermal curves the solid phases are individual salts, while at the isothermal invariant points they are mixtures of salts. All the data on our research into the $K_2Cr_2O_7 - K_2SO_4 - H_2O$ system are collected in Table 1 and plotted graphically in Fig. 1.

In describing the effect of other salts upon the solubility of any given salt, it is best to employ the comparative analysis of mutual solubility in a series of ternary aqueous salt systems.

We made this comparison, based on the mutual solubility at 20°, for the following systems: $K_2Cr_2O_7 - KCl - H_2O$ [2], $K_2Cr_2O_7 - KBr - H_2O$ [1], $K_2Cr_2O_7 - KNO_3 - H_2O$ [2], $K_2Cr_2O_7 - K_2SO_4 - H_2O$.

The solubility equilibrium diagrams are simple ones in these systems. The composition of the solutions is governed by the ions that make up the crystalline structures of the salts. All the systems have the same cation and a common salt component. The differing ions are all anions.

In this instance, the problem may be reduced to a comparison of the monovariant crystallization curves of potassium dichromate with the respective solubility isotherms.

This comparison is based upon the following assumptions.

1. In a three-component system, a solution that is not saturated with one of the components may be regarded as a new solvent with respect to the component with which the solution is saturated [3]. Hence, the monovariant isothermal curves can describe the solubility of the saturated salt solution in the presence of varying amounts of the other salt.

2. Dissolution and crystallization depend upon the singularities of the crystalline structure of a salt,

TABLE 1

Point	Per cent by weight			Molecular per cent			Solid phase
No.	H_2O	$K_2Cr_2O_7$	K_2SO_4	H_2O	$K_2Cr_2O_7$	K_2SO_4	
				20° Isotherm			
1	88.9	11.1	–	99.24	0.76	–	K_2Cr_2O
2	88.82	10.16	1.02	99.19	0.69	0.12	
3	88.69	9.91	1.40	99.16	0.68	0.16	
4	88.60	9.53	1.87	99.13	0.65	0.22	
5	88.06	8.56	3.38	99.02	0.59	0.39	
6	87.78	7.80	4.42	98.95	0.53	0.52	
7	86.67	6.92	6.41	98.76	0.48	0.76	
8	85.53	6.24	8.23	98.58	0.44	0.98	$K_2Cr_2O_7 + K_2SO_4$
9	86.10	5.42	8.48	98.62	0.34	1.00	K_2SO_4
10	86.91	4.20	8.89	98.67	0.29	1.04	
11	87.49	3.08	9.43	98.69	0.21	1.10	
12	88.38	1.98	9.64	98.77	0.11	1.12	
13	89.65	0.45	9.90	98.85	0.03	1.13	
14	90.0	–	10.0	98.87	–	1.13	
				25° Isotherm			
1	86.92	13.08	–	99.08	0.92	–	$K_2Cr_2O_7$
2	86.35	12.09	1.56	98.97	0.85	0.18	
3	85.91	11.14	2.95	98.86	0.79	0.35	
4	85.73	10.12	4.15	98.79	0.71	0.50	
5	85.05	9.15	5.80	98.65	0.65	0.70	
6	84.29	7.70	8.01	98.48	0.55	0.97	
7	84.24	7.43	8.33	98.46	0.53	1.01	$K_2Cr_2O_7 + K_2SO_4$
8	84.66	6.69	8.65	98.48	0.48	1.04	
9	85.05	6.15	8.80	98.51	0.44	1.05	K_2SO_4
10	86.37	4.03	9.60	98.59	0.28	1.13	
11	86.95	3.13	9.92	98.62	0.22	1.16	
12	87.62	2.28	10.10	98.65	0.17	1.18	
13	88.31	1.19	10.50	98.70	0.09	1.21	
14	88.56	0.74	10.70	98.72	0.05	1.23	
15	89.20	–	10.80	98.76	–	1.24	
				30° Isotherm			
1	84.6	15.4	–	98.90	1.10	–	$K_2Cr_2O_7$
2	83.98	13.16	2.86	98.70	0.95	0.35	
3	83.14	12.20	4.66	98.54	0.89	0.57	
4	82.66	11.39	5.95	98.44	0.83	0.73	
5	82.10	10.15	7.75	98.30	0.74	0.96	
6	81.59	9.75	8.66	98.20	0.72	1.08	
7	81.52	9.41	9.07	98.18	0.69	1.13	$K_2Cr_2O_7 + K_2SO_4$
8.	83.45	6.80	9.75	98.32	0.49	1.19	
9	85.31	4.54	10.15	98.47	0.32	1.21	K_2SO_4
10	86.12	3.48	10.40	98.53	0.24	1.23	
11	86.32	2.94	10.74	98.52	0.21	1.27	
12	87.09	1.76	11.15	98.57	0.12	1.31	
13	87.71	1.01	11.28	98.62	0.07	1.31	
14	88.52	–	11.48	98.68	–	1.32	
				40° Isotherm			
1	79.4	20.6	–	98.44	1.56	–	$K_2Cr_2O_7$

TABLE 1 - (continued)

Point No.	Per cent by weight			Molecular per cent			Solid phase
	H_2O	$K_2Cr_2O_7$	K_2SO_4	H_2O	$K_2Cr_2O_7$	K_2SO_4	
40° Isotherm							
2	79.38	19.45	1.17	98.37	1.48	0.15	$K_2Cr_2O_7$
3	79.36	18.94	1.80	98.33	1.44	0.23	
4	78.81	17.65	3.54	98.20	1.35	0.45	
5	78.71	16.89	4.40	98.14	1.29	0.57	
6	78.49	15.98	5.53	98.07	1.22	0.71	
7	78.13	15.24	6.63	97.97	1.17	0.86	
8	77.63	14.61	7.76	97.86	1.13	1.01	
9	77.40	14.40	8.20	97.81	1.12	1.07	$K_2Cr_2O_7 + K_2SO_4$
10	79.46	11.66	8.88	97.99	0.88	1.13	K_2SO_4
11	80.50	9.90	9.60	98.05	0.74	1.21	
12	81.65	8.30	10.05	98.14	0.61	1.25	
13	82.68	6.88	10.44	98.22	0.50	1.28	
14	83.60	5.60	10.80	98.29	0.40	1.31	
15	84.02	4.45	11.43	98.30	0.32	1.38	
16	84.44	3.71	11.85	98.31	0.26	1.43	
17	85.10	2.70	12.20	98.35	0.19	1.46	
18	85.18	2.46	12.36	98.35	0.17	1.48	
19	85.70	1.84	12.46	98.39	0.13	1.48	
20	85.90	1.34	12.76	98.36	0.13	1.51	
21	86.72	0.34	12.94	98.46	0.02	1.52	
22	86.9	–	13.1	98.47	–	1.53	

which are governed by the fundamental nature and type of the chemical bond within the crystals for every solid [4]. Therefore, under the given thermodynamical conditions, the formation of solid phases in heterogeneous systems is largely governed by the available possibilities in the field of the chemical bond that can be actually realized in the formation of a stable crystalline structure. From the energy standpoint, this process is generally characterized by such interaction among the crystal's structural units (ions, atoms, and molecules) as will result in the system having a minimum energy.

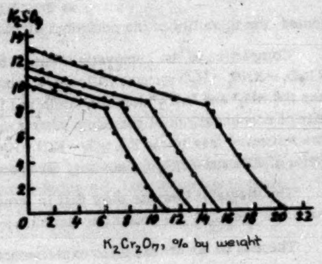

Figure 1

3. The process of crystallization of a salt from a dilute ternary solution by isothermal evaporation, as well as the establishment of a state of equilibrium by the addition of another salt to a saturated solution of the given salt, are best related to a given value of the solution's ionic strength. In the comparative evaluation of mutual solubility, the ionic strength gives a fuller characterization of such a property as, say the solubility of a given salt in the presence of other salts than the solution concentration does, since using the ionic strength makes it possible to relate the change in solubility of the given salt in various ternary systems to the change in the solution structure due to the substitution of one noncommon ion for another.

Figure 2 is a general diagram of the solubility isotherms at 20° for the four systems specified above.

We see from this diagram that the crystallization branches for potassium dichromate in the $K_2Cr_2O_7 - KBr - H_2O$ and $K_2Cr_2O_7 - KCl - H_2O$ systems, which contain substances that are similar from the standpoint of crystal chemistry as the second salt components, are of the same type. These branches determine the nature of the equilibria prevailing in both systems, whereas the crystallization branches for the KBr and KCl are of practically no importance, inasmuch as the solubilities of these salts in isothermally invariant solutions are practically the same as their individual solubilities. Hence, it may be stated that in the ternary solutions used for comparison, containing the spherical Cl' or Br' anions as the noncommon ions in combination with the complex Cr_2O_7'' anion, the structural and energy conditions are such as to lower the individual solubility of the salt component with the more complicrystal structure considerably. Moreover, aqueous solutions of such substances as KCl and KBr may be regarded as equivalent aqueous salt solvents for potassium dichromate.

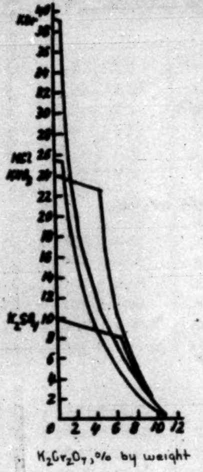

Figure 2.

The salt series KCl (KBr), KNO_3, K_2SO_4, and $K_2Cr_2O_7$, which are the constituents of the systems under comparison, exhibits a comparative comlication of crystal structure. As we have stated above, the first two salts are crystallochemically alike. Their isomorphism, in the narrow sense of the term, is a matter of common knowledge. The last three salts differ from the first two, as well as differing from one another, in point of the structural data pertaining to the complex anions, since in such salts as KNO_3, K_2SO_4, and $K_2Cr_2O_7$, structure is largely determined by the form and dimensions of the complex anion, which, in turn, depend upon the nature of the chemical bond and the coordination between the cation and the anion within the coordinated group.

Therefore, the noncommon anions in our ternary systems have structures of varying complexity: Cl' and Br' are spherical anions; NO_3' is triangular; SO_4'' is tetrahedral; the structure of Cr_2O_7'' is not yet definitely established, though this anion is apparently one of the pyro-ions of the S_2O_7'' type, with the general shape of $O_nA-O-AO_m$ [5].

Pursuing the comparison of the cited solubility isotherms on a crystallochemical basis, we may set down the general conclusion that as the crystal structure of the second salt components grows more complicated, the solubility of the potassium dichromate in the respective ternary systems increases.

Comparison of the monovariant curves for potassium dichromate in the $K_2Cr_2O_7-KCl-H_2O$ and $K_2Cr_2O_7-KNO_3-H_2O$ systems indicates a substantial increase in the solubility of the potassium dichromate when the NO_3' and Cr_2O_7'' ions are combined in ternary solutions. We see from this comparison that the range of concentrations of potassium nitrate solutions in which potassium dichromate can be dissolved is more restricted than in the $K_2Cr_2O_7-KCl-H_2O$ system, notwithstanding the fact that the individual solubilities of KCl and KNO_3 are not very far apart.

The diagrams likewise show that in ternary solutions in which the concentrations of the second salt component are alike the potassium dichromate is more soluble in solutions that contain potassium nitrate.

There is no doubt that these experimental data may be interpreted so that the change in the structure and energy of potassium dichromate in the $K_2Cr_2O_7-KNO_3-H_2O$ system, relative to the $K_2Cr_2O_7-KCl-H_2O$ system, depends largely upon the structure of the NO_3' ion: its form, dimensions and charge.

The combination of such large and structurally complicated anions as SO_4'' and Cr_2O_7'' in the ternary solutions of the $K_2Cr_2O_7-K_2SO_4-H_2O$ system is less favorable for the crystallization of potassium dichromate, so that the solubility of this salt is higher than in the systems considered previously. Potassium sulfate exhibits only slight salting-out action with respect to potassium dichromate, and both salts crystallize out together when the concentration of potassium sulfate is only slightly higher in the isothermal invariant solution. The combined action of the two salts diminishes their nearly similar individual solubilities to values that are not very far from, say, those in the $K_2Cr_2O_7-KCl-H_2O$ system.

As we have stated above, we combined a study of a property such as the solubility of a given salt in solutions containing varying compositions of other salts with an allowance for the ionic strengths of the solutions at which the salts crystallized. Let us assume that we have a solution of the $K_2Cr_2O_7-KBr-H_2O$

system that is dilute with respect to both of the salts, with a given value of ionic strength and a definite ratio of the ionic strengths of the salts making up the system. Say, this ratio is unity, for example. When such a solution is evaporated isothermally, the points representing its composition will all lie on a straight line connecting the water vertex of the diagram to a certain point on the monovariant crystallization curve for potassium dichromate (Figure 3). The transition from a solution that is unsaturated with respect to one salt to a saturated solution involves the establishment of a solid phase. This phase formation occurs at a certain value of the solution's ionic strength, the given ratio between the summand values of the salts' ionic strengths remaining unchanged.

In the 20° isotherm we have reproduced, the potassium dichromate crystallizes all the way up to the isothermal invariant point throughout a wide range of values for the ratio of the ionic strength of the saturating salt's solution to the ionic strength of the nonsaturating salt's solution, the overall ionic strength of the solution increasing uninterruptedly. We see from the composition of the isothermal invariant solution that increasing the concentration of potassium bromide in the ternary solutions results in the nearly complete salting-out of the potassium dichromate. Hence, the interaction between ions and between ions and molecules of the solvent in ternary solutions of the $K_2Cr_2O_7 - KBr - H_2O$ system is such as to cause almost total replacement of the potassium dichromate by the potassium bromide. It is useful to describe such interaction between particles in solution as regards such a property as the solubility of the freely soluble salt in various water-salt solvents by definite values of the ionic strength, even if only in the most general manner.

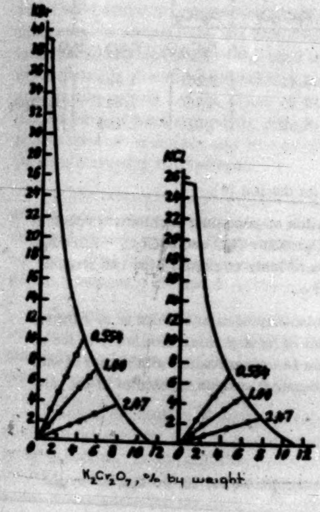

Figure 3

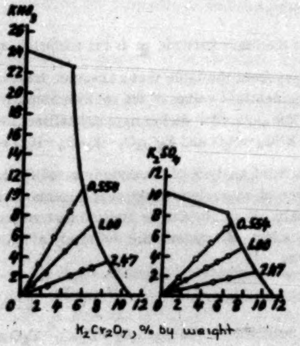

Figure 4

Figures 3 and 4 are diagrams of the 20° isotherms for the four solutions under comparison, with three rays representing the following ratios of the ionic strength of the potassium dichromate to the ionic strength of the respective other salt: 3.47; 1; and 0.554. The underlying numerical figures for these diagrams are listed in Table 2.

The ratio of the ionic strengths of the salts is denoted by the letter a in the table. The solution ionic strengths were calculation from the equation:

$$\mu = \frac{1}{2}\left(m_1 z_1^2 + m_2 z_2^2 + \ldots\right)$$

TABLE 2

Value of $\underline{a}$	Grams per 100 g of saturated solution		Solution ionic Strength	Solid phase	Grams per 100 g of saturated solution		Solution ionic Strength	Solid phase
	$K_2Cr_2O_7$	KBr			$K_2Cr_2O_7$	KCl		
	$K_2Cr_2O_7-KBr-H_2O$				$K_2Cr_2O_7-KCl-H_2O$			
2.47	8.06	3.96	1.312	$K_2Cr_2O_7$	7.99	2.46	1.279	$K_2Cr_2O_7$
1.00	6.00	7.28	1.411		6.17	4.69	1.411	
0.554	4.53	9.92	1.514		4.80	6.60	1.551	
	$K_2Cr_2O_7$	KNO_3			$K_2Cr_2O_7$	K_2SO_4		
	$K_2Cr_2O_7-KNO_3-H_2O$				$K_2Cr_2O_7-K_2SO_4-H_2O$			
2.47	8.49	3.54	1.383	$K_2Cr_2O_7$	9.41	2.26	1.521	$K_2Cr_2O_7$
1.00	6.85	7.05	1.621		7.90	4.70	1.847	
0.554	5.90	10.97	2.03		6.56	7.01	2.169	

where μ is the ionic strength, $\underline{m}$ is the molarity, and $\underline{z}$ is the charge on the ion [6].

We see from the table that at certain values of $\underline{a}$ the crystallization of potassium dichromate occurs at practically identical values of the solution ionic strength in the $K_2Cr_2O_7-KBr-H_2O$ and $K_2Cr_2O_7-KCl-H_2O$ systems. The potassium dichromate crystallizes at other, higher values of ionic strength in the two systems $K_2Cr_2O_7-KNO_3-H_2O$ and $K_2Cr_2O_7-K_2SO_4-H_2O$ at the same values of $\underline{a}$.

This brief analysis of the experimental findings on the mutual solubility of salts enables us to estimate the presence of equivalent water-salt solvents for a given salt by means of its structural similarity to the respective salts. It might also be stressed that various instances of change in the individual solubilities of salts in ternary water-salt systems are definitely affected by the crystallochemical structural features of the salt components.

SUMMARY

1. Solubility in the $K_2Cr_2O_7-K_2SO_4-H_2O$ system has been investigated at 20, 25, 30 and 40° by the methods of physicochemical analysis.

2. It has been shown that it is possible to systematize the experimental data on mutual solubility in ternary water-salt systems by allowing for the crystallochemical structural data of the salts.

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THE KINETICS OF CINNAMIC ACID HYDROGENATION

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The rate of catalytic hydrogenation of a dissolved substance that is continuously agitated with a finely pulverized catalyst in a current or an atmosphere of nitrogen by the method first employed by Fokin [1], depends upon the temperature, the concentration of the solute, the nature of the solvent, the hydrogen pressure in the gas phase, the nature of the bond to be hydrogenated, the presence of other efficiently adsorbing groups in the molecule, the degree of substitution of the bond to be hydrogenated (the screening), the quantity of catalyst, the activity and the nature of the catalyst, and the rate of stirring (number of oscillations). An equation has recently been derived for the velocity of hydrogenation that allows for the existence of a semihydrogenated state at the surface and for two kinds of surface — one activating the substance to be hydrogenated and the other activating the hydrogen.

Of the factors listed above, the following determine the operational procedure: temperature, hydrogen pressure, solute concentration, nature of the solvent, quantity of the catalyst, activity and nature of the catalyst, and rate of stirring. There are only scattered papers dealing with the interrelated study of all or at any rate most of the kinetic factors specified. Most papers deal with an investigation of the effect of a single factor, most frequently the nature of the catalyst.

The rate of catalytic hydrogenation in the liquid phase may be described by equations ranging from zero order to the second order, depending upon the process conditions, the nature of the substance undergoing hydrogenation, and the nature of the catalyst. We often come across fractional orders, as well as instances of the order of reaction changing in the course of the process.

Many of the authors of papers on catalytic hydrogenation in the liquid phase have not paid enough attention to the need for making a distinction between the "diffusion" and the "kinetic" regions in the hydrogenation process. In the diffusion region, the hydrogenation velocity is governed by the rate of diffusion of the initial substances, the unsaturated compound and the hydrogen, toward the catalyst's surface or of the reaction products into the solution. In the kinetic region one of the processes occurring directly at the surface is the stage that limits the overall velocity. Whether a given process takes place in the kinetic or the diffusion region is determined by the process conditions: temperature, pressure, stirring rate, and quantity of catalyst [2, 3]. At least 250-300 oscillations of the hydrogenation apparatus must be ensured for the hydrogenation reaction to take place in the " kinetic" region.

Elovich and Zhabrova [4] have made a detailed study of how the stirring rate affects the kinetics of hydrogenating styrene in glacial acetic acid over Pt/$BaSO_4$.

Our research has dealt with a study of the kinetics of hydrogenation over a nickel catalyst, prepared by leaching out a 50% nickel-aluminum alloy with lime and called " skeletonized nickel". We used apparatus of our own design, with precise temperature control and very intensive stirring [3, 5].

OPERATIONAL PROCEDURE

The major parts of the installation were the gas buret, fitted with a water jacket to keep the temperature constant, and the hydrogenation device proper — the "duck". The duck was attached to holes in a coupling and was brought into strong and regular motion by a 0.25 kw motor; the oscillations of the duck could be varied from 200 to 1600 per minute. The oscillation length was variable, but it was 5.2 cm as a rule. The number of oscillations was checked by measuring the rpm. The duck was oscillated in a water thermostat (0.1 m^3), fitted with a stirrer and a thermoregulator. The variation of temperature within the thermostat did not exceed ± 0.1°. The duck was immersed in the thermostat up to its stopcock, so that all its contents were beneath the level of the water. The size of the apparatus enabled us to attach two ducks to the coupling at the same time, thus running parallel tests.

A three-way stopcock was used to connect the gas buret either to a gasometer containing hydrogen or to the duck. Water was used as the sealing fluid in the buret. The hydrogen was produced by electrolyzing a 20% solution of NaOH, using platinum or nickel electrodes. The traces of oxygen were removed from the hydrogen in a furnace, using platinized asbestos or metallic copper, while the traces of sulfur compounds were removed by passing the hydrogen through an alkaline solution of plumbite.

A sample of the substance (from 0.1 to 0.2 g) was transferred to the duck by means of a solvent, a weighed amount of the catalyst was added, and then some more of the solvent.[1]

Then the air was driven out of the system by passing large volumes of hydrogen (ranging from 0.5 to 1.0 liter) through it or by alternately pumping out the duck and filling it with hydrogen (testing the hydrogen for purity after evacuation).

The starting of the agitation motor was fixed as the start of the run, with the amount of hydrogen taken from the gas buret recorded against a stop watch. The runs lasted from 3 minutes to several hours. The end of hydrogenation was determined by the absence of any change in the water level within the buret during the course of several minutes.

The order in which the various constituents were introduced into the duck was varied, the exact order being stated in the text each time. Whenver catalysts or the substance to be hydrogenated were added during the course of the run, the motor was disconnected, the operation continuing in a current of hydrogen.

Cinnamic acid was chosen as the test substance. In our subsequent experiments cinnamic acid has served as a reference standard for comparing the hydrogenation rates of various organic compounds. Commerical cinnamic acid, recrystallized twice from distilled water, was dried at 105°; its m.p. was 132.5°.

The catalyst was prepared from an alloy containing 50% Ni and 50% Al.

After several tests, we settled upon the following procedure for preparing an activated catalyst: 1 g of the alloy, finely pulverized in a mortar, was placed in a flask fitted with a reflux condenser, which contained 80 ml of an NaOH solution that had been first heated on a boiling water bath. Leaching on the water bath lasted two hours, after which the alkali was decanted, and the catalyst was washed by decanting it four times with 100-ml portions of distilled water and twice with alcohol (20 ml). In this washing some of the light particles of the catalyst are lost, and its activity is diminished appreciably. To prevent loss, all the wash waters were poured into a single bottle, the small quantity of catalyst particles that settled with time being separated by another decantation and then combined with the bulk of the catalyst, the whole being transferred to the duck. It is even better to decant the bulk of the wash waters and then to centrifuge the remainder.

In one of our tests, the catalyst, consisting of 1 g of alloy, was washed with 400 ml of water and 20 ml of 95% alcohol, transferred to a U-shaped tube and dried in a current of hydrogen. The catalyst then weighed 0.565 g.

Experiment No. 1. 0.5 gram of cinnamic acid was dissolved in 15 ml of 95% alcohol and placed in a duck; the catalyst (0.56 g) was added, together with another 10 ml of alcohol. The air was driven out of the duck by hydrogen, and the motor was started as soon as the solution to be hydrogenated had reached the temperature of the thermostat. The thermostat temperature was 25° (±0.1°), the temperature of the water in the jacket of the measuring buret being 10°. The pressure (p) was 697.5 mm; the "duck" was oscillated back and forth 330 times per minute; and the length of the "duck" travel was 5.2 cm.

As this experiment shows, the reaction rate is satisfactorily described by an equation for a first-order reaction. The velocity constant, calculated graphically, was 0.051. Hydrogenation is complete, and a drop in the velocity constant is observed only after 65 ml of hydrogen (*i.e.*, more than 3/4) had been absorbed. The velocity rate is very low when no stirring is used or when the number of oscillations is low; at upward of 300-330 duck oscillations per minute, however, the reaction rate at 25° is practically independent of any further increase in the stirring rate. This is indicated by the figures in Table 2.

The reaction remains a first-order one as the stirring rate is increased and the temperature is varied. This enables us to calculate the apparent activation energy of the hydrogenation of cinnamic acid in alcohol solution over skeletonized Ni. The activation energy, as calculated from the formula:

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[1] The dimensions of the duck enabled us to vary the total liquid volume from 10 to 50 ml.

TABLE 1

Experiment 1

Time, Minutes	V_2	$\frac{\Delta V_2}{\Delta t}$	$\frac{\Sigma V_2}{2}$	Time, Minutes	V_2	$\frac{\Delta V_2}{\Delta t}$	$\frac{\Sigma V_2}{2}$
0	0.0	5.6	2.8	17	58.6	2.1	59.6
1	5.6	4.7	8.0	18	60.7	2.1	61.8
2	10.3	4.6	12.6	19	62.8	2.0	63.8
3	14.9	4.2	17.0	20	64.8	1.7	65.6
4	19.1	3.7	21.0	21	66.5	1.6	67.3
5	22.8	3.7	24.6	22	68.1	1.4	68.8
6	26.5	3.5	28.2	23	69.5	1.4	70.2
7	30.0	3.5	31.8	24	70.9	1.0	71.4
8	33.5	3.3	35.2	25	71.9	1.1	72.3
9	36.8	3.3	38.4	26	73.0	0.8	73.4
10	40.1	3.0	41.6	27	73.8	0.7	74.2
11	43.1	2.5	44.4	28	74.5	0.5	74.8
12	45.6	2.9	47.0	29	75.0	0.24	75.6
13	48.5	2.8	49.9	34	76.2	0.16	76.6
14	51.3	2.5	52.6	39	77.0	0.0	77.0
15	53.8	2.5	55.0	44	77.0	0.0	77.0
16	56.3	2.3	57.4	49	77.0	–	–

TABLE 2

Variation of the Rate of Hydrogenation of Cinnamic Acid with the Number of Duck Oscillations

Hydrogenation conditions: 0.5 g of cinnamic acid; 25 ml of 95% alcohol as the solvent; catalyst prepared from 1 g of 50% alloy.

Test No.	Temperature	Oscillations per minute (back and forth)	K
1 (7)	25°	330	0.051
2 (8)	25	440	0.044
3 (5)	25	550	0.048
4 (9)	25	650	0.047
		Average	0.0475
The same behavior pattern is repeated at 0°			
5 (11)	0	300	0.010
6 (12)	0	300	0.010
7 (13)	0	400	0.011
8 (10)	0	440	0.013
		Average. . . .	0.0115

TABLE 3

Variation of the Rate of Hydrogenation of Cinnamic Acid with the Volume of Solvent

Hydrogenation conditions: 0.5 g of cinnamic acid; catalyst prepared from 1 g of alloy

Test No.	Ml of alcohol	K
7	15	0.012
6	25	0.012
8	50	0.011

$$E = \frac{RT_1T_2}{T_2 - T_1} 2.3 \log \frac{K_2}{K_1} \sqrt{T_1/T_2}$$

was found to be 9108 ±1000 cal per mole.

It was found that the velocity constant remained the same when the concentration of cinnamic acid was varied (varying the volume of solvent from 15 to 50 ml), though keeping the catalyst quantity constant and keeping the rate of agitation constant at a sufficiently high level (Table 3).

We also investigated the variation of the rate of hydrogenation of cinnamic acid with the quantity of catalyst used, varying the latter from 1 to 4 g, based on the Ni-Al alloy. The catalyst was washed out, with the washings centrifuged. The respective data are to be found in Table 4.

It may therefore be regarded as certain that the hydrogenation rate is directly proportional to the quantity of catalyst (q) within the range investigated.

TABLE 4

Variation of the Rate of Hydrogenation of Cinnamic Acid with the Quantity of Catalyst Used (Based on the Alloy)

Hydrogenation conditions: 25 ml of 95% alcohol; 400 oscillations per minute; 0°; 0.5 g of cinnamic acid.

Test No.	Quantity of alloy	Method of leaching and washing	K	K/q
9	2.00	At once...............	0.038	0.019
6	1.00	At once...............	0.010	0.010
20	3.00	At once...............	0.056	0.019
11	2	In 1-g batches.......	0.022	0.011
12	1	With centrifuging...	0.010	0.010
21	4	In 2-g batches.......	0.072	0.018

Our method of preparing the catalyst yielded a rather active catalyst, with not unsatisfactory reproducibility of the tests; this was reinforced by the results of a special study on the variation of the activity of skeletonized Ni with the extent and duration of leaching. We leached out 1 g of the alloy on a boiling water bath for 5, 15, 30, 60, 75, 90, 120, 150, 180, 240, 360 minutes and more. Different quantities of hydrogen were evolved, corresponding to these intervals of time. As before, each catalyst sample was washed four times with distilled water and twice with alcohol. The results of these tests are listed in Table 5.

The catalyst was leached out for 6 hours 30 minutes on a boiling water bath and then allowed to stand in the alkali for 15 hours at room temperature.

TABLE 5

Variation of the Activity of a Ni Catalyst with the Extent and Time of Leaching

Leaching conditions: 80 ml of 20% alkali; 1 g of alloy; temperature: boiling water bath. Hydrogenation conditions: 24°; 0.5 g of cinnamic acid; 25 ml of 95% alcohol as solvent; 400 oscillations per minute; oscillation length 5.2 cm; dimensions of duck – 3.7 X 14 cm.

Leaching time, minutes..................	5	15	30	60	75	90	120	150	180	240	360
Volume of hydrogen evolved during leaching out of the alloy, ml.........	375	415	500	660	675	715	715	715	715	715	715
Relative hydrogenation rate during the first five minutes	1.7	1.7	2.1	2.7	3.2	2.7	2.4	2.4	2.4	2.4	2.4

We see that the activity of the catalyst remained unchaged after two hours of leaching, while the catalyst did not cake after prolonged heating at 100°. The production of maximum catalyst activity by leaching, as established in our research, supports the incomplete leaching of an Ni-Al alloy proposed by several authors [6].

It is therefore fully advisable to leach out the Ni-Al alloy partially in preparing a catalyst, after which it is activated by releaching as its activity falls off. Using this procedure, we can hydrogenate a substantial quantity of cinnamic acid without producing any perceptible change in catalyst activity; when pure hydrogen and cinnamic acid are employed, there is only little change in the activity of skeletonized Ni after 3 or 4 successive runs.

SUMMARY

1. A study has been made of the effect of stirring upon the kinetics of the hydrogenation of cinnamic acid dissolved in 96% ethyl alcohol over skeletonized Ni.

2. It has been found that cinnamic acid is hydrogenated in the "kinetic" region, the process being unaffected by any increase in the stirring rate over 300 oscillations of the duck per minute.

3. It has been found that the reaction is of the first order for cinnamic acid. The activation energy of the process has been found to be 9000 ± 1000 cal per mole.

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THE ELECTROCHEMICAL OXIDATION OF ANILINE IN THE PRESENCE OF CATALYSTS

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The assertion is made in various foreign patents [1] that aniline can be quantitatively oxidized to quinone electrochemically in solution when certain compounds are present.

In order to explore the effect of the presence of catalysts in the solution upon the electrochemical oxidation of aniline we ran a series of experiments on the electrochemical oxidation of sulfuric acid solutions of aniline with Mn, Cr, V, and Ce compounds, using platinum and lead electrodes.

We likewise investigated the kinetics of the anodic processes, using polarization curves.

EXPERIMENTAL

The apparatus used for electrolysis was set up in accordance with the layout usually employed for this purpose. The electrolyzer was a half-liter chemical glass beaker, inside which there was placed a 0.2-liter porous ceramic beaker. The glass beaker served as the cathode space. The ceramic beaker served as the anode space and as a diaphragm separating the cathode and anode spaces.

Cylindrical electrodes were used. The anode used was either a mesh made of 1-mm platinum wire, with a total surface of 13.5 cm^2, or a perforated lead plate, with a working surface of 200 cm^2. The cathode was a lead plate with a working surface of 280 cm^2.

The electrolyzer was connected in series with a coulometer and a milliammeter. The current source was a lead storage battery connected to a high-resistance rheostat. By means of the latter the required external voltage was taken from the storage battery and led to the electrolyzer. During electrolysis the anode potential was continuously checked, being kept within a certain range by regulating the external voltage. A saturated calomel electrode served as the reference electrode for measuring the anode potential. The electrode potential was measured by means of the customary compensation circuit, using a P-4 potentiometer.

When we plotted the polarization curves, we conducted electrolysis in the glass beaker without using the ceramic diaphragm. We used helical electrodes made of 1-mm platinum wire. The cathode was placed within a long glass tube 15 mm in diameter, set up vertically in the beaker with its lower edge 3-4 mm from the bottom of the beaker. In this setup intensive stirring with a mechanical stirrer was employed during electrolysis.

Analine, refined by double distillation with zinc dust, was employed in all our tests.

In electrolysis we used 0.3 molar (Pb anode) and 0.1 molar (Pt anode) solutions of aniline in 1.5-molar sulfuric acid containing compounds of one of the following elements: Mn, Cr, V, or Ce. Electrolysis was stopped after a certain quantity of electricity had passed through the solution, as determined by the coulometer.

A solid ranging in color from green to dark-green, plus some quinone, was produced in the anode space, depending upon the electrolysis conditions. The solid was separated from the liquid in a vacuum filter. The solution was extracted with ether. The ether was evaporated. The ether extract was combined with the solid residue and then distilled with steam. The percentage of quinone in the aqueous solution produced by steam distillation was determined iodometrically. The solid residue was thoroughly washed, first with soda and then with water, then separated from the liquid on a vacuum funnel, and dried at 100-110°. Its yield was determined by weighing. The dried product did not fuse at temperatures below 320°.

Experimental Results and Their Evaluation

The figure shows the polarization curves giving the current density as a function of the anode potential, plotted in the presence of Mn, Cr, V, and Ce compounds.

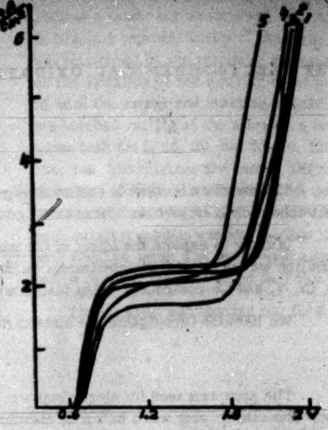
The anode potential, plotted as the abscissas, is the emf of the cell, consisting of the polarized electrode and the saturated calomel half-cell; it includes the potential jump at the liquid contact.

In all the cases we have investigated the polarization curve consisted of two branches. Under the conditions corresponding to the lower branch of the polarization curve nothing occurs during electrolysis but the oxidation of aniline at the anode. No oxygen or quinone is produced under these circumstances.

Under the electrolysis conditions corresponding to the upper branch of the polarization curve, the aniline is oxidized and oxygen is evolved, while a dark solid product is formed in the anodic region, together with a small amount of quinone.

Inspection of the polarization curves reproduced in the figure indicates that the presence of small amounts of Mn, Cr, V, or Ce has no appreciable effect upon the nature of the polarization curves, and, hence, upon the kinetics of the current-generating process.

The principal results of our experiments on the electrolysis of solutions of aniline in sulfuric acid with platinum and lead electrodes, as well as the experimental conditions employed, are given in Tables 1 and 2, respectively.



Polarization curves of aniline dissolved in sulfuric acid. 1) Without a catalyst; 2) Ce; 3) Cr; 4) V; 5) Mn.

Examination of the results listed in Tables 1 and 2 shows that small yields of quinone were secured in some instances when the aniline was oxidized. The quinone yield was higher when Mn, Cr, V, and Ce compounds were present (and a platinum electrode was used) than in the absence of these compounds. These elements differ somewhat in the degree to which they promote the yield of quinone.

TABLE 1
Electrolysis of Sulfuric Acid Solutions of Aniline with a Platinum Anode

Oxygen carrier	Anode potential, volts, referred to saturated calomel electrode	Amt. electricity passed through Ah	Yield of black aniline, g.	Yield of quinone, g.
None	2.0-2.2	4.3	1.12	0.026
$MnSO_4$ 0.067 m	1.7-2.1	3.15	1.8	0.21
	1.7-2.1	3.3	1.8	0.27
NH_4VO_3 0.067 m	2.1-2.5	2.1	–	0.03
	2.2-2.5	3.5	0.95	0.109
	2.1-2.5	4.1	0.88	0.084
$Cr(SO_4)_3$ 0.067m	2.0-2.2	1.2	–	0.013
	2.0-2.2	4.1	–	0.084
CeO_2 0.067 m	2.35-2.50	4.3	1.09	0.167
	2.85-2.50	2.1	0.950	0.107
	2.35-2.50	4.8	–	0.164

TABLE 2
Electrolysis of Sulfuric Acid Solutions of Aniline with a Lead Anode

Oxygen carrier	Anode potential, volts, referred to saturated calomel electrode	Amt. electricity passed through Ah	Yield of black aniline, g.	Yield of quinone, g.
None	1.5	6.35	5.7	0
None	1.5-1.8	7.8	5.0	0
None	1.5	11.5	4.90	Traces
HVO_3 0.3 m	1.5-1.8	5.5	5.5	0
HVO_3 0.3 m	1.5-2.0	6.8	5.7	0.05
HVO_3 0.3 m	1.5-2.0	13.6	1.0	0.32
$MnSO_4$ 1.5 m . . .	1.5-2.0	5.8	4.3	0
$MnSO_4$ 1.5 m . . .	1.5-2.2	2.7	2.8	0
$Cr_2(SO_4)_3$ 1 m . .	1.5	8	4	0
$Cr_2(SO_4)_3$ 1.5 m ..	1.5-1.9	8	5.3	0.

When a lead anode is used, quinone is formed only when vanadium compounds are present.

SUMMARY

A series of experiments has been run on the electrochemical oxidation of solutions of aniline in sulfuric acid containing compounds of Mn, Cr, V, and Ce, and it has been shown that these compounds increase the yield of quinone.

LITERATURE CITED

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Received June 11, 1950

THE PRODUCTION OF ORTHOTITANIC ACID ESTERS BY THE RE-ESTERIFICATION METHOD

B. A. Arbuzov and Z. G. Isaeva

Bischoff and Adkins [1] were the first to produce orthotitanic acid esters in the pure state, by reacting titanium tetrachloride with alcoholates. They secured a 67% yield of the tetraethyl ester, and 80% yields of the isopropyl and tetrabutyl esters.

They produced the tetramethyl ester by reacting tetraethyl orthotitanate with methanol. Tetraethyl orthotitanate has been produced by this method by other authors as well [2]. There are references in the patent literature to the production of titanium acid esters by the reaction of alcohols with titanium tetrachloride in the presence of nitrogen bases that bind the hydrogen chloride [3].

In our investigation of ortho acid esters by the method of dipole moments and parachors we found it necessary to synthesize esters of orthotitanic acid with the higher alcohols. In contrast to the patent data, we were unable to produce orthotitanic acid esters by reacting titanium tetrachloride with alcohols in the presence of dimethylaniline. Synthesis of orthotitanic acid esters by the action of alcoholates of the higher alcohols upon titanium tetrachloride is difficult, owing to the necessity of using large quantities of the higher alcohols to prepare alcoholate solutions, which led us to employ the re-esterification method to produce orthotitanic acid esters containing long alkyl radicals.

In producing the higher esters of orthotitanic acid, we used tetraethyl orthotitanate, which we succeeded in preparing from the alcoholate and titanium tetrachloride in absolute alcohol, the yield being 70% of the theoretical, provided the reagents were thoroughly protected against moisture.

The re-esterification of the ethyl ester with higher alcohols readily gave us high yields of the butyl, hexyl, octyl, and nonyl esters of orthotitanic acid as viscous liquids, faintly yellow in color, the constants of which were as follows:

TABLE

Ester	Yield,% of theoretical	B.p.	d_4^{20}	n_D^{20}
n-Butyl	76	166° (6.5 mm)	1.0051	1.4925
n-Hexyl	85.9	201-204 (2 mm)	0.9573	1.4830
n-Octyl	84.1	255-258 (2 mm)	0.9339	1.4810
n-Nonyl	77.9	264-265 (1.5 mm)	0.9241	1.4785

The hexyl, octyl, and nonyl esters have not been described previously in the literature.

After this research had been completed and the dipole moments of the synthesized esters had been measured [4], there appeared a paper by Speer [5], in which he describes the synthesis of several esters of orthotitanic acid by the action of titanium tetrachloride upon the alcoholates of the respective alcohols in benzene (the ethyl, n-propyl, n-butyl, isobutyl, sec-butyl, and n-octyl esters) and by a re-esterification reaction (tert-butyl ester). Like us, Speer was also unable to secure orthotitanic acid esters in the presence of nitrogen bases (dimethylaniline, pyridine, ammonia). The yields of orthotitanic esters secured by Speer were lower than those we secured by re-esterification.

EXPERIMENTAL

Synthesis of the butyl ester of orthotitanic acid. 10.6 g of the ethyl ester of orthotitanic acid, with a b.p. of 149-151° (11 mm), and 21 g (a 52% excess) of n-butyl alcohol were placed in an A.E. Arbuzov flask, and the flask was heated slowly. Ethyl alcohol was driven off, as was the excess of butyl alcohol in vacuo, and the residue was distilled. This yielded 10.2 g of orthobutyl titanate with a b.p. of 166° (6.5 mm), or 76% of the theoretical yield.

The orthotitanic acid ester was analyzed by saponifying a sample of the ester with water in a crucible at 30-35° and drying the resultant titanium oxide to constant weight in the flame of a soldering torch.

0.1314 g, 0.1144 g substance: 0.0314 g, 0.0268 g TiO_2. Found %: Ti 14.32, 14.04. $C_{16}H_{36}O_4Ti$. Calc.%: Ti 14.09.

Synthesis of the n-hexyl ester of orthotitanic acid. We used 6.5 g (0.028 mole) of the ethyl ester of orthotitanic acid and 11.6 g , (0.113 mole) of hexyl alcohol in this reaction. The mixture was heated in an A.E.Arbuzov flask until no more ethyl alcohol was driven off. Distillation of the residue in vacuo yielded 9.8 g of the hexyl ester of orthotitanic acid, with a b.p. of 201-204° (2 mm), the yield being 85.9% of theoretical.

0.1304 g, 0.1000 g substance: 0.0222 g, 0.0174 g TiO_2. Found %: Ti 10.19, 10.43. $C_{24}H_{52}O_4Ti$. Calculated %: Ti 10.59.

Synthesis of the n-octyl ester of orthotitanic acid. We used 4.1 g of ethyl orthotitanate and 10.2 g of n-octyl alcohol. Driving off the ethyl alcohol and vacuum distillation yielded 8.5 g (84.1% of the theoretical yield) of octyl orthotitanate, with a b.p. of 255-258 g (2 mm).

0.1178 g, 0.1074 g substance: 0.0164 g, 0.0148 g TiO_2. Found %: Ti 8.35, 8.26. $C_{32}H_{68}O_4Ti$. Calculated %: Ti 8.49.

Synthesis of the n-nonyl ester of orthotitanic acid. We used 3.5 g ethyl orthotitanate and 10 g of n-nonyl alcohol. Driving off the ethyl alcohol and vacuum distillation yielded 7.4 g of a dark-red product, which turned light-yellow when allowed to stand for two days in a sealed ampoule. B.p. 264-265° (1.5 mm). Yield 77.9% of the theoretical.

0.1324 g, 0.1598 g substance: 0.0168 g, 0.0200 g TiO_2. Found %: Ti 7.61, 7.50. $C_{36}H_{76}O_4Ti$. Calculated %: Ti 7.73.

SUMMARY

High yields of the following esters of orthotitanic acid have been synthesized by the re-esterification of the ethyl ester of orthotitanic acid: the n-butyl, n-hexyl, n-octyl, and n-nonyl esters.

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Received July 2, 1950

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THE RAMAN SPECTRA OF SOME TERPENE HYDROCARBONS

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The Raman spectra of many terpenes have been investigated more than once. When we compare the findings of various authors, however, we find great discrepancies, due to the preparations not being pure enough and to inaccuracies in frequency measurements. To be sure, satisfactory results may be obtained in the spectral analysis of products containing terpenes only if we have accurate and reliable data on the spectra of absolutely pure preparations of the individual compounds. The securing of such data is an indispensable step in achieving the effective spectral analysis of systems that contain complicated molecules, the spectra of which contain a very large number of lines.

The literature contains many papers on the spectroscopic investigation of mixtures of terpenes. Valuable data were secured in papers by Pigulevsky and others [1,2] on the composition of turpentine, which demonstrated that it was entirely possible to secure accurate spectra and to decipher them. The results of such investigations can be made even more complete provided we have accurate data on the spectra of the pure hydrocarbons.

We cite below the results of determinations of the Raman spectra of three terpenes: α-pinene, Δ^3-carene, and limonene, isolated in as pure a state as possible from pine turpentine. The spectra were photographed with a three-prism spectrograph equipped with glass optics with a linear dispersion of 27 Å/μμ. The 4358.3 Å mercury line, separated by means of light filters, was used as the spectrum excitation. The spectra were recorded by photographing them on isochromatic photographic plates of average sensitivity. The slit width of the spectrograph was 5 cm^{-1}. The line frequencies were calculated by means of interpolation formulas, applying corrections determined from the standards of the iron-arc spectrum. Three optimum-exposure spectra were secured for each substance tested. The accuracy of frequency measurement was $\pm$ 1 cm^{-1} for the clear lines. The line intensities were determined visually on the basis of a 10-point scale. All the hydrocarbons we investigated were redistilled in vacuo without boiling in a sealed glass apparatus before photographing the spectra in order to free them of fluorescing impurities and suspended micro-particles.

Spectrum of d-α-pinene. This hydrocarbon was isolated from pine turpentine by carefully fractionating the latter in vacuo into a column with an efficiency of 50 theoretical trays and a reflux ratio of 40. The purest fractions of the α-pinene we secured were redistilled under the same conditions. We used the fraction that possessed the following constants:

d_4^{20} 0.8578; n_D^{20} 1.4653; $[\alpha]_C$ 22.30°; $[\alpha]_D$ 28.46°; $[\alpha]_{Hg_j}$ 29.76°; $[\alpha]_{Hg_i}$ 56.71°; $\frac{\alpha_V}{\alpha_C}$ 1.132; $\frac{\alpha F}{\alpha_C}$ 1.969 for our research.

To judge from the physical properties, this fraction is the purest α-pinene; it yielded a very clear spectrum containing 45 lines:

207(3); 261(6,b); 305(5); 337(1)*; 388(5); 426(5); 464(5); 483(5); 566(7); 618(6); *667(10); 735(0)*; 771(7); 790(0); 819(3); 843(8); 888(3)*; 908(6); 929(3); 943(3); 954(6); 994(1)*; 1014(1); 1043(6); 1065(1); 1086(7); 1126(7); 1165(7); 1182(6)*; 1205(4); 1221(5); 1265(7); 1306(5); 1331(7); 1376(6); 1436(8); 1449(6); 1471(3); 1658(9s); 2836(7); 2875(8); 2920(9); 2958(7); 2990(8); 3027(6).

As against the previously known data, we have discovered 6 new lines. The rather good agreement of our data with the findings of G. Pigulevsky [1] is worthy of note. The line frequencies for α-pinene found by us differ from the findings of Dupont [3] and of Nevgi [4], being 4-5 cm^{-1} below the Dupont figures and about 3-4 cm^{-1} above the Nevgi figures.

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* The asterisks denote new lines in this spectrum as well as in the subsequent ones.

Spectrum of d-Δ^3-carene. Most of the research workers who have worked with Δ^3-carene have expressed doubt about the purity of the tested samples of this hydrocarbon, but they have been unable to free it of the impurities it contained. Nor can the samples of Δ^3-carene secured from pine turpentine prepared from trees growing on the territory of the USSR be considered wholly free from impurities.

It may be now regarded as certain that the so-called carene fraction consists of two major components: d-Δ^3-carene and a hydrocarbon that we formerly called d-terpene [5]. By repeated fractionation into a column with an efficiency of 50 theoretical trays we have succeeded in separating the Δ^3-carene from its accompanying hydrocarbon, which is concentrated in the first runnings. The sample of pure Δ^3-carene thus produced had the following physical constants:

B.p. 169.5-170.5° at 746 mm; n_D^{20} 1.4723; d_4^{20} 0.8645; $[\alpha]_C$ 13.03°; $[\alpha]_D$ 17.08°; $[\alpha]_{Hg_j}$ 18.00°; $[\alpha]_{Hg_i}$ 38.76°; α_V/α_j 1.154; α_F/α_C 2.179.

The Raman spectrum proved to be a very clear one, exhibiting 34 lines of the following frequencies:

244(3)*; 342(3); 407(5,b)*; 422(5,b); 502(5); 569(5); 679(8); 713(10); 757(6); 785(4); 819(9); 937(8); 977(3)*; 988(3)*; 1034(5)*; 1071(3)*; 1101(4); 1143(3)*; 1156(5); 1201(4)*; 1226(5); 1306(5); 1367(5); 1379(5); 1416(4)*; 1439(10); 1469(4); 1685(10); 2830(5); 2870(8); 2903(8); 2930(8); 2965(3); 3004(10).

The presence of new lines in the spectrum, not observed by other authors and denoted by an (*) should be noted. Some of these lines are rather strong. We also resolved the components of duplets that had been assumed to be single lines (such as 1156 and 1143, 1379 and 1367. Notwithstanding the high intensity and clarity of the spectrum recorded, we were unable, however, to detect a line in the 1640 region, which has been noted by all previous authors in the spectrum of Δ^3-carene. It follows from structural considerations, however, that the vibrational spectrum of the Δ^3-carene molecule actually ought to contain only a single band in the 1600-1700 cm^{-1}; this is the 1685 cm^{-1} band. There is therefore every reason to suppose that the 1640 line belonged to an impurity of another hydrocarbon, which was eliminated from our sample of Δ^3-carene.

A comparison of our frequencies with the Pigulevsky and Ryskalchuk findings [1] shows that they are in good agreement; greater discrepancies exist between our figures and those of Nevgi [4] and Dupont [3], amounting to as much as 12 cm^{-1}, which indicate the inaccuracies in the measurements made by these authors. In our opinion, the frequency values given in this paper are the most accurate data for Δ^3-carene.

Spectrum of the low-boiling fraction. We endeavored, by means of repeated careful fractionation of the carene fraction, to isolate from it a low-boiling hydrocarbon that would differ from β-pinene and Δ^3-carene in its characteristically low value of specific gravity. The isolation of this hydrocarbon in the pure state is a difficult task, because its boiling point differs but little from the boiling point of Δ^3-carene. The fraction that we isolated was free of Δ^3-carene. Its physical constants were as follows:

n_D^{20} 1.4723; d_4^{20} 0.8401; $[\alpha]_C$ 8.01°; $[\alpha]_D$ 10.60°; $[\alpha]_{Hg_j}$ 11.20°; $[\alpha]_{Hg_i}$ 25.45°; α_V/α_j 1.160; α_F/α_C 2.248.

The Raman spectrum of the fraction was as follows:

293(2); 350(3,b); 410(2); 425(4); 505(3); 570(3); 650(2); 680(6); 715(7); 759(4); 790(2); 822(5); 903(4)*; 940(5); 980(1); 990(1); 1008(1)*; 1040(1); 1070(3); 1103(3); 1145(1); 1153(4); 1202(2); 1229(4); 1297(7)*; 1380(6); 1419(5,b); 1438(9,b); 1635(12)*; 1678(7)*; 1687(3); 2830(5); 2870(8); 2898(8); 2924(8); 2967(5); 3007(8); 3090(3)*;

We see that there are 3 lines, 1687, 1678, and 1635, in the double-bond region. The first frequency is that of the double bond in Δ^3-carene, the presence of which is also evident from the existence of nearly all the other lines of this compound in the spectrum. The very strong 1635 line belongs to another unsaturated hydrocarbon; its high intensity (evaluated by comparison with the 1710 line for acetone in an acetone solution) is at least 100 units [8], indicating that conjugated double bonds are present in the molecule of this hydrocarbon. The much weaker 1678 line evidently belongs to an unconjugated double bond. The spectrum of the fraction contains a total of 6 lines that do not belong to Δ^3-carene [they are denoted by an (*)]. The strongest of these lines, 903, 1297, 1635, 1678, and 3090, coincide with the characteristic lines of myrcene. The spectrum of the latter actually exhibits a very strong line for conjugated double bonds (1636) and a weaker line for a single double bond (~1675). Comparison of the line intensities enables us to conclude that about 1/3 of the tested fraction consists of Δ^3-carene, the rest consisting chiefly of myrcene.

Spectrum of limonene. The following samples were tested: a mixture of l-limonene and dipentene, isolated as the result of careful fractionation of pine turpentine oil, which we have called l-limonene for short; a mixture of d-limonene and dipentene, isolated from dry-distilled pine tar oil and called d-limonene by us; and, lastly, dipentene produced by the thermal isomerization of α-pinene by the Arbuzov method [6]. The physical properties of these samples are listed in the appended table. The spectra of the samples of limonene and dipentene isolated by us are in fairly good agreement with each other and agree, at least qualitatively, with the figures in the literature. The following lines were found in the limonene spectrum:

305(2); 330(2); 342(1); 428(4); 488(2); 520(3); 543(2); 641(4); 681(0); 702(2,b); 760(8); 785(1); 798(6,b); 816(0); 889(5); 917(4); 956(1); 1015(3,b); 1054(3); 1078(3); 1110(3); 1154(4,b); 1209(3); 1250(0); 1276(2); 1292(2); 1309(2); 1332(1); 1374(5,b); 1392(0); 1433(6); 1454(4); 1644(7); 1676(7); 2835(5); 2858(3); 2872(4); 2912(8,b); 2927(4); 2966(5); 2981(2); 3013(2); 3080(2).

Sample	d_4^{20}	n_D^{20}	$[\alpha]_D$
l-Limonene.......	0.8443	1.4750	−82.3°
d-Limonene.......	0.8444	1.4772	+ 10.20
Dipentene.........	0.8435	1.4734	+ 0.98

The precise values of the double-bond frequencies of 1644 and 1676 differ from the figures given by Dupont and some other authors, though they approach the values given by Yatkar. In addition to the specified lines, the following lines were found in the spectrum of the dipentene prepared by the B.A.Arbuzov method: 1632(3); 1588(3); 1574(1); 1238(4); and 1185(3). These lines doubtless belong to alloöcimene, which is present as an impurity (totaling about 1%) in the given sample of dipentene.

Let us mention that the present research again confirms the fact that most of the so-called "l-terpene", a constant component of Russian turpentine oils, consists of limonene, with the l-isomer predominating [7].

SUMMARY

The Raman spectra of the pure terpenes secured from native pine turpentines: α-pinene, limonene, and Δ^3-carene, have been investigated.

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Received May 12, 1950.

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SUMMARY

The [illegible] effects [illegible] have been investigated.

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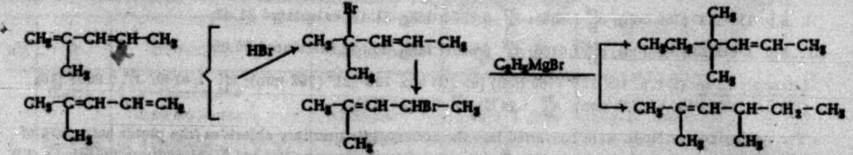
Received May 15, 196[illegible]

SYNTHESIS OF HYDROCARBONS

XX. SYNTHESIS OF ALKENES AND ALKANES CONTAINING A QUATERNARY CARBON ATOM

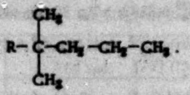
R. Ya. Levina, T. I. Tantsyreva, and A. A. Fainzilberg

The reaction of ethylmagnesium bromide with the hydrobromide of 2- or 4-methylpentadiene-1,3, which reacts in two isomeric forms, results, as we have shown previously [1], in the formation of a mixture of two isomeric alkenes (70% of the theoretical yield): 4,4-dimethylhexene-2 and 2,4-dimethylhexene-2, the former constituting 40% of the alkene mixture:



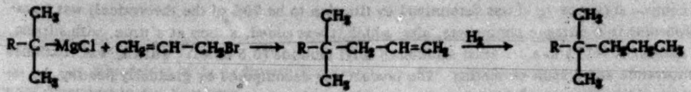
The isomeric alkanes, 2,4-dimethylhexane and 3,3-dimethylhexane, produced in the hydrogenation of the resulting alkene mixture, were separated by fractionation into a column.

The same series of reactions in which other organomagnesium compounds (n-propylmagnesium bromide, isopropylmagnesium bromide, and n-butylmagnesium bromide) were used resulted in the formation of a mixture of alkanes, which included homologs of 3,3-dimethylhexane—alkanes containing a quaternary carbon atom—the general structure of which is:



$$R-C(CH_3)_2-CH_2-CH_2-CH_3.$$

For the purposes of identification (by the Ramán spectrum method), each of these alkanes had to be synthesized by another method. Hydrocarbons of this structure can be synthesized by employing a reaction of allyl bromide with the respective tert-alkylmagnesium chloride, followed by hydrogenation of the products of this reaction— α-ethylenic hydrocarbons that contain a quaternary carbon atom (4,4-dimethylalkenes-1).



$$R-C(CH_3)_2-MgCl + CH_2=CH-CH_2Br \longrightarrow R-C(CH_3)_2-CH_2-CH=CH_2 \xrightarrow{H_2} R-C(CH_3)_2-CH_2CH_2CH_3$$

The reaction of tert-alkylmagnesium chlorides with an allyl halide has been described in several papers as a method of synthesizing 4,4-dimethylalkenes-1. Whitmore [2], for example, secured a high yield of 4,4-dimethylpentene-1 (R = CH_3) by reacting tert-butylmagnesium chloride with allyl bromide at 5°, and by adding the two reagents in the inverse order. When the reaction is carried out under ordinary conditions, the hydrocarbon yield drops to 5% of the theoretical [3]. Liberman and Kazansky [4], employing allyl chloride instead of the bromide and carrying out the reaction at 12-16°, secured 35% of the theoretical yield of 4,4-dimethylhexene-1 (R = C_2H_5).

In the present paper 4,4-dimethylheptene-1 (R = n-C_3H_7, 49% of the theoretical yield), 4,4,5-trimethylhexene-1 (R = iso-C_3H_7, 28% of the theoretical yield), and 4,4-dimethyloctene-1 (R = n-C_4H_9, 42% of the theoretical yield) have been synthesized by reacting the tert-alkylmagnesium chlorides with allyl bromide, the corresponding alkanes — 4,4-dimethylheptane, 2,3,3-trimethylhexane, and 4,4-dimethyloctane — being produced by hydrogenating the foregoing alkenes. The synthesized hydrocarbons distilled within a narrow temperature range — 0.1 to 0.2° (into a column with an efficiency of 35 theoretical trays), with the exception of 4,4-dimethylheptene-1, which distilled in a 0.4° range.

Of the six synthesized hydrocarbons, two hydrocarbons (4,4-dimethyloctene-1 and 4,4-dimethyloctane, $C_{10}H_{20}$ and $C_{10}H_{22}$) are not described in the literature. Nor has the synthesis of the other four hydrocarbons (C_9H_{18} and C_9H_{20}) been described in the literature; the constants of three of them are given, however, in the handbooks of Egloff and Doss, with references to unpublished dissertations by Reid [5,6] and Kline [6], while Fenske [7] cited some constants (b.p. and n_D^{20}) of the fourth hydrocarbon (without describing or even mentioning the method of synthesis) in a paper on Raman spectra.

EXPERIMENTAL

The initial tertiary alcohols were prepared by reacting absolute acetone [8] with organomagnesium compounds (n-propylmagnesium bromide, isopropylmagnesium bromide, and n-butylmagnesium bromide). Acetone was added while the reaction mixture was chilled with ice; then the reaction mixture was heated and stirred for 3 hours and allowed to stand overnight; it was decomposed by pouring over ice and adding dilute (15%) acetic acid; the aqueous layer was extracted 5 times with ether. The alcohols produced: dimethylpropylcarbinol (I), dimethylisopropylcarbinol (II), and dimethylbutylcarbinol (III), their yields being 54, 41, and 71% of the theoretical, respectively, had the following constants:

I. B.p. 120.3° (770 mm); n_D^{20} 1.4087; d_4^{20} 0.8041; MR_D 31.40; calculated 31.43.

II. B.p. 117-118° (750 mm); n_D^{20} 1.4235; d_4^{20} 0.8294; MR_D 31.41; calculated 31.43.

III. B.p. 138-139° (742 mm); n_D^{20} 1.4185; d_4^{20} 0.8136; MR_D 36.04; calculated 36.05.

Literature data: (I) b.p. 122-123° (760 mm) [9]; (II) b.p. 120-121° (762 mm); n_D^{18} 1.4140; d_4^{20} 0.8208 [10]; (III) b.p. 139.4-140.4° (735 mm); n_D^{20} 1.4175; d_4^{20} 0.8119 [11].

The synthesized carbinols were converted into the corresponding tertiary chlorides (the yields being 80% of the theoretical): 2-chloro-2-methylpentane (IV), 2-chloro-2,3-dimethylbutane (V), and 2-chloro-2-methylhexane (VI) by the action of concentrated hydrochloric acid upon the icewater-chilled reagent (the reaction mixture was kept in the same chilling agent for 1.5 hours after the hydrochloric acid had been added). The constants of the synthesized chlorides were as follows:

IV. B.p. 105-107° (746 mm); n_D^{20} 1.4128; d_4^{20} 0.8610; MR_D 34.90; calculated 34.78.

V. B.p. 108-109° (760 mm); n_D^{20} 1.4212; d_4^{20} 0.8758; MR_D 34.93; calculated 34.78.

VI. B.p. 127-128° (753 mm); n_D^{20} 1.4193; d_4^{20} 0.8569; MR_D 39.69; calculated 39.39.

Literature data: (IV) b.p. 110-113° (760 mm); $n_D^{16.5}$ 1.4148; d_4^{15} 0.8678 [12]; (V) b.p. 112° (749 mm); d_4^{15} 0.8784 [13]; (VI) b.p. 130-135° (760 mm) [14].

Synthesis of 4,4-dimethylalkenes-1 (C_9H_{18} and $C_{10}H_{20}$). 2 ml of ethyl bromide was added to 12 g of magnesium, activated by heating with iodine and covered with 150 ml of absolute ether, to start the reaction, after which a 1:1 ether solution of the tertiary chloride (0.5 mole) was gradually added at a rate that did not exceed one drop per second. The reaction flask had to be gently heated to keep the ether boiling gently but evenly; after the chloride had been added, heating was continued until all the magnesium had disappeared. The ether solution of the organomagnesium compound (whose yield was determined by titration to be 70% of the theoretical) was transferred to a funnel by siphoning in a nitrogen atmosphere, after which it was added, a drop at a time, with stirring and chilling (external chilling to −11°) to a 1:1 ether solution of allyl bromide (0.5 mole). Stirring was continued for 2 hours at room temperature and 3 hours of heating. The product was decomposed by gradually pouring the reaction mixture over ice to which ammonium chloride had been added. After the ether extract had been processed in the usual manner and the ether had been driven off, the residue was heated with sodium and distilled over the sodium twice. The alkenes thus purified, which contained not a trace of halogen, were distilled over sodium into a column with an efficiency of 35 theoretical trays. The constants and yields* of the synthesized alkenes are given in Table 1. The figures in the literature are cited in Table 4.

4,4-Dimethylheptene-1: 5.745 mg substance: 18.010 mg CO_2; 7.405 mg H_2O. 6.070 mg substance: 19,035 mg CO_2; 7.800 mg H_2O. Found %: C 85.55, 85.60; H 14.43, 14.48. C_9H_{18}. Calc. %: C 85.71; H 14.29.

4,4-Dimethyloctene-1: 7.520 mg substance: 23.585 mg CO_2; 9.720 mg H_2O. 5.480 mg substance: 17.180 mg CO_2; 7.050 mg H_2O. Found %: C 85.59, 85.55; H 14.46, 14.40. $C_{10}H_{20}$. Calc.%: C 85.62; H 14.38.

Bromination of the synthesized 1-alkenes was effected in a chilled chloroform solution. After the reaction mixture had been processed in the usual manner and the chloroform had been driven off, the dibromides

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* Based on the tertiary chloride.

TABLE 1

Constants of Alkenes with the General Structure of $RC(CH_3)_2CH_2CH=CH_2$

No.	R	Alkene	Boiling point	n_D^{20}	d_4^{20}	MR_D		Yield	
						Found	Calculated	(g)	% of theoretical
1	C_3H_7	4,4-Dimethylheptene-1	129.1-129.5° (764 mm)	1.4185	0.7324	43.45	43.30	31	49
2	iso-C_3H_7	4,4,5-Trimethylhexene-1	132.2-132.4° (760 mm)	1.4251	0.7494	43.10	43.30	17.5	28
3	C_4H_9	4,4-Dimethyloctene-1	152.5-152.6° (749 mm)	1.4231	0.7451	47.94	47.91	30	42

TABLE 2

Constants of Dibromides with the General Structure of $RC(CH_3)_2CH_2CHBrCH_2Br$

No.	R	Dibromide	Boiling point	n_D^{20}	d_4^{20}	MR_D	
						Found	Calculated
1	C_3H_7	1,2-Dibromo-4,4-dimethylheptane	87.5-88° (3 mm)	1.4972	1.4070	59.54	59.29
2	iso-C_3H_7	5,6-Dibromo-2,3,3-trimethylhexane	90.5-91 (3 mm)	1.5046	1.4320*	59.24	59.29
3	C_4H_9	1,2-Dibromo-4,4-dimethyloctane	101 (3 mm)	1.4942	1.3590	64.31	63.91

TABLE 3

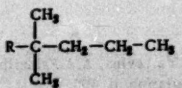
Constants of Alkanes with the General Structure of $RC(CH_3)_2CH_2CH_2CH_3$

No.	R	Alkane	Boiling point at 760 mm	n_D^{20}	d_4^{20}	MR_D	
						Found	Calculated
1	C_3H_7	4,4-Dimethylheptane	134.3-134.4°	1.4076	0.7221	43.74	43.76
2	iso-C_3H_7	2,3,3-Trimethylhexane	136.2-136.4	1.4138	0.7323	43.73	43.76
3	C_4H_9	4,4-Dimethyloctane	157.4-157.6	1.4144	0.7347	48.44	48.38

were distilled in vacuo; the constants of the resultant dibromides are given in Table 2.

The dibromides of 4,4-dimethylheptene-1, 4,4,5-trimethylhexene-1 and 4,4-dimethyloctene-1 are not described in the literature.

Synthesis of Alkanes (C_9H_{20} and $C_{10}H_{22}$) with the Structure of



$$\mathrm{R-\overset{CH_3}{\underset{CH_3}{C}}-CH_2-CH_2-CH_3}$$

The alkenes were hydrogenated over platinized charcoal (15% platinum) at 160°. The constants of the synthesized alkanes after distillation over sodium into a column with an efficiency of 35 theoretical trays is given in Table 3. The figures in the literature are cited in Table 4.

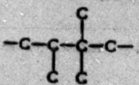
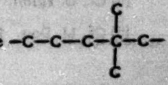
We see from the figures in Tables 1 and 3 that in each pair of isomers, C_9H_{18} (Nos. 1 and 2) and C_9H_{20} (Nos. 1 and 2), (where R = n-C_3H_7 and iso-C_3H_7), the hydrocarbons with a more highly branched structure, containing the  $\mathrm{-C-\underset{C}{C}-\overset{C}{\underset{C}{C}}-C-}$ group, possess higher constants than the isomeric hydrocarbons with the  $\mathrm{-C-C-C-\overset{C}{\underset{C}{C}}-C-}$ structure.

TABLE 4

Data in the Literature

No.	Hydrocarbon	B.p.	n_D^{20}	d_4^{20}	Remarks
1	4,4-Dimethylheptene-1	130.0-130.7° (740 mm)	1.4175	0.7489	Quoted from Egloff's handbook [5]; not described in the periodical literature.
2	4,4,5-Trimethylhexene-1	133.7-134.7 (760 mm)	1.4230	0.7528	Ditto
3	4,4-Dimethyloctene-1	—	—	—	Not described in the literature
4	4,4-Dimethylheptane	135.2 (760 mm)	1.4076	—	[7]
5	2,3,3-Trimethylhexane	137.4-137.6 (760 mm)	1.4141	0.7374	Quoted from Doss's handbook [6]; not described in the periodical literature.
6	4,4-Dimethyloctane	—	—	—	Not described in the literature

Hence, the isomeric hydrocarbons we have synthesized exhibit the characteristic pattern of behavior in the changes of their physical properties that is present, to judge by the data in the literature, in the isomeric hydrocarbons C_8H_{16} [15] (3,3-dimethylhexene-1 and 3,3,4-trimethylpentene-1) and C_8H_{18} [16] (3,3-dimethylhexane and 2,3,3-trimethylpentane), which have similarly branched carbon skeletons.

SUMMARY

1. Three ethylenic hydrocarbons with a quaternary carbon atom—4,4-dimethylpentene-1, 4,4,5-trimethylhexene-1, and 4,4-dimethyloctene-1 — have been synthesized by reacting tertiary alkylmagnesium chloride with allyl bromide, the yields being 49, 28, and 42% of the theoretical, respectively, based on the original tertiary chloride.

2. The synthesized alkenes have been identified as their dibromides (not described in the literature).

3. Alkanes with a quaternary carbon atom (C_9H_{20} and $C_{10}H_{22}$) — 4,4-dimethylheptane, 2,3,3-trimethylhexane, and 4,4-dimethyloctane—have been produced by hydrogenating the synthesized alkenes catalytically.

4. All the synthesized hydrocarbons have been collected within a narrow temperature range (0.1-0.2°, the range being 0.4° in only one instance) after distillation into a column with an efficiency of 35 theoretical trays and have been determined by accurate constants.

5. 4,4-Dimethyloctene-1 and 4,4-dimethyloctane have not been described in the literature. Only incomplete constants (b.p. and n_D^{20}) are cited in the literature for 4,4-dimethylheptane, without a description, or even a mention of the method of synthesis employed. The other hydrocarbons have not been published in the periodical literature, their constants being found only in handbooks, with references to unpublished foreign dissertations.

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July 19, 1950

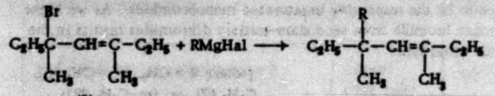
The N.D.Zelinsky Laboratory of Organic Chemistry
of the M.V.Lomonosov State University of Moscow,
Awarded the Order of Lenin.

SYNTHESIS OF HYDROCARBONS

XXI. HYDROBROMIDES OF DIENES IN THE SYNTHESIS OF OLEFINS AND PARAFFINS WITH A QUATERNARY CARBON ATOM

R.Ya.Levina and N.P.Shusherina

In our preceding report [1] we described the reaction of organomagnesium compounds (methylmagnesium iodide and ethylmagnesium bromide) with the unsaturated tertiary bromide 5-brom-3,5-dimethylheptene-3 (I), the structure of which excludes the possibility of any allyl rearrangement:



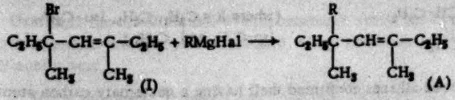
$$C_2H_5\underset{CH_3}{\overset{Br}{C}}-CH=\underset{CH_3}{C}-C_2H_5 + RMgHal \longrightarrow C_2H_5-\underset{CH_3}{\overset{R}{C}}-CH=\underset{CH_3}{C}-C_2H_5$$

(I) (where R = CH_3 and C_2H_5)

The structure of the products of this reaction— the unsaturated hydrocarbons 3,5,5-trimethylheptene-3 and 3,5-dimethyl-5-ethylheptene-3 — was established by oxidizing them. Hydrogenating these synthesized alkenes yielded the respective alkanes— 3,3,5-trimethylheptane and 3,5-dimethyl-3-ethylheptane—their possession of a quaternary carbon atom being demonstrated by an analysis of their Raman spectra. Thus, the reaction of the tertiary allylic bromide 5-bromo-3,5-dimethylheptene-3 with organomagnesium compounds proved to be a convenient method of synthesizing hydrocarbons that are difficult of access and are not described in the literature: the 3,5-dimethyl-5-ethylalkenes-3 (the yield being 30% of the theoretical), and from them their corresponding alkanes.

In the present paper this reaction has been utilized to synthesize alkenes of higher molecular weight: two dodecenes and two tridecenes, hydrogenation of these alkenes yielding the corresponding dodecanes and tridecanes.

The reaction of 5-bromo-3,5-dimethylheptene-3 (I) with propyl-, isopropyl-, butyl-, and isobutylmagnesium bromides synthesized the following alkenes with a quaternary carbon atom that have not been described in the literature: 3,5-dimethyl-5-ethyloctene-3; 3,5,6-trimethyl-5-ethylheptene-3; 3,5-dimethyl-5-ethylnonene-3; and 3,5,7-trimethyl-5-ethyloctene-3. The corresponding aromatic and cyclohexane hydrocarbons containing allylic side chains: 3,5-dimethyl-5-phenylheptene-3 and 3,5-dimethyl-5-cyclohexylheptene-3, which have not been described in the literature



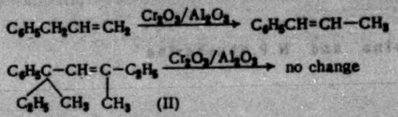
$$C_2H_5\underset{CH_3}{\overset{Br}{C}}-CH=\underset{CH_3}{C}-C_2H_5 + RMgHal \longrightarrow C_2H_5\underset{CH_3}{\overset{R}{C}}-CH=\underset{CH_3}{C}-C_2H_5$$

(I) (A)

(where R = C_3H_7, C_4H_9, iso-C_3H_7, iso-C_4H_9, C_6H_5, C_6H_{11})

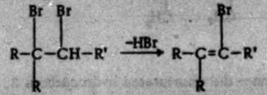
have likewise been synthesized by reacting the same tertiary allylic bromide (I) with phenylmagnesium bromide and cyclohexylmagnesium chloride.

The presence of a quaternary carbon atom between the double bond and the radical R in the synthesized hydrocarbons of the general structure (A) was established by the behavior of one of them (R = C_6H_5), 3,5-dimethyl-5-phenylheptene-3 (II), a homolog of allylbenzene, in a contact isomerization reaction. As one of the present authors has demonstrated previously, allylbenzene and its homologs readily undergo a characteristic conversion into propenylbenzene and its homologs, whose physical and chemical properties differ considerably from those of the initial hydrocarbons when placed in contact with alumina [2] and chromic oxide on alumina [3] at 250°. If there is a quaternary carbon atom deprived of a hydrogen located between the double bond and the aromatic radical, the double bond cannot be shifted, of course. As a matter of fact, when 3,5-dimethyl-5-phenylheptene-3 was passed over chromic oxide on alumina (at 250°), it did not suffer any isomerization, which is direct confirmation of the structure of this hydrocarbon and, hence of the cited hydrocarbons of structure (A), synthesized in the same reaction:



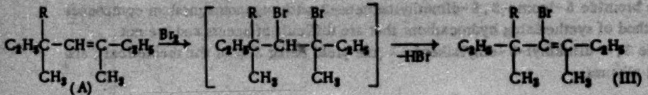
The structure of the synthesized alkenes was likewise confirmed by analyzing the oxidation products of two of them: 3,5-dimethyl-5-ethyloctene-3 and 3,5-dimethyl-5-ethynonene-3.

Large amounts of hydrogen bromide were liberated when the alkenes were brominated in an ether solution; the products of this reaction proved to be the respective unsaturated monobromides. As we know from the literature, the splitting out of hydrogen bromide from secondary-tertiary dibromides results in the formation of unsaturated monobromides of the vinyl type:



(where R = CH_3, R' = CH_3 [6], C_2H_5 [7] or iso-C_3H_7 [8])

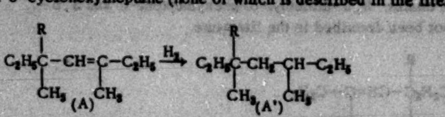
Thus, the unsaturated dibromides that are the products of the bromination of the isomeric alkenes synthesized in the present research are apparently homologs of vinyl bromide (III):



(where R = C_3H_7, iso-C_3H_7, C_4H_9, iso-C_4H_9)

The specific nature of the bromination reaction is borne out by the structure of the synthesized alkenes as trisubstituted ethylenes (containing the —CH=C< group).

Hydrogenation of the synthesized alkenes, and of the cyclohexane hydrocarbon with an unsaturated side chain, resulted in the synthesis of the corresponding alkanes (A'): 3,5-dimethyl-5-ethyloctane; 2,3,5-trimethyl-3-ethylheptane; 3,5-dimethyl-5-ethylnonane; 2,4,6,-trimethyl-4-ethyloctane, and 3,5-dimethyl-3-cyclohexylheptane (none of which is described in the literature):



(where R = C_3H_7, C_4H_9, iso-C_3H_7, iso-C_4H_9, and C_6H_{11})

Examination of the Raman spectra of the synthesized alkanes confirmed their having a quaternary carbon atom.

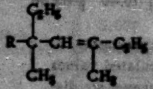
EXPERIMENTAL

The initial tertiary allyl bromide, 5-bromo-3,5-dimethylheptene-3 (I), was produced by adding one molecule of hydrogen bromide at the 1,2 and 1,4 positions to a mixture of dienes: 3,5-dimethylheptadiene-2,4 and 4-methyl-2-ethylhexadiene-1,3. The synthesis and analysis of the initial dienes and the synthesis of the hydrobromide (I) from them have been described in preceding reports [1,4].

Synthesis of unsaturated hydrocarbons with a quaternary carbon atom (A). 5-Bromo-3,5-dimethylheptene-3 (I) was reacted with organomagnesium compounds (RMgHal, where R = C_3H_7, iso-C_3H_7, C_4H_9, iso-C_4H_9, C_6H_5, and C_6H_{11}) under the conditions we have described previously [1] (for the reaction of this bromide with methylmagnesium iodide), i.e., with the proportions of 5-bromo-3,5-dimethylheptene-3 to the alkyl halide and the magnesium being 1:1.5:1.5, employing constant stirring and chilling of the reaction mixture at −40 to −50°, followed by its heating for 6 hours. The products of the reaction of the initial unsaturated hydrobromide (I) with the propyl-, isopropyl-, butyl-, and isobutyl-magnesium bromides were processed in the usual manner and then fractionated* over sodium into a column with an efficiency of 25 theoretical trays. The products of the reactions of the hydrobromide (I) with the phenylmagnesium bromide* and the cyclohexylmagnesium chloride were distilled (over sodium) in vacuo, after the low-boiling fractions* had been driven off at atmospheric pressure. The allylbenzene homolog (II), produced in the first of these reactions (R = C_6H_5), was freed of its traces of diphenyl by freezing it twice before the vacuum distillation. The constants and the yields of the synthesized unsaturated hydrocarbons (A) are given in Table 1, the analysis data being given in Table 4.

TABLE 1

Hydrocarbons of the General Structure



$R-C(C_2H_5)(CH_3)-CH=C(CH_3)-C_2H_5$

Where R is	Name of hydrocarbon	B.p.	n_D^{20}	d_4^{20}	MR_D		Yield, % of theoretical
					Found	Calc.	
C_3H_7	3,5-Dimethyl-5-ethyloctene-3	191.4° (756 mm)	1.4432	0.7800	56.96	57.17	40
iso-C_3H_7	3,5,6-Trimethyl-5-ethylheptene-3	194.5-195 (754 mm)	1.4492	0.7913	56.61	57.17	27
C_4H_9	3,5-Dimethyl-5-ethylnonene-3	211.5-212 (766 mm)	1.4457	0.7850	61.85	61.76	41
iso-C_4H_9	3,5,7-Trimethyl-5-ethyloctene-3	206.5-207.5 (765 mm)	1.4446	0.7833	61.77	61.76	30
C_6H_5	3,5-Dimethyl-5-phenylheptene-3	104-104.5 (4 mm) 255-256 (755 mm)	1.5313	0.9244	67.75	67.40	18
C_6H_{11}	3,5-Dimethyl-5-cyclohexylheptene-3	97-97.5 (1.5 mm)	1.4790	0.8660	68.23	68.00	41

Oxidation of the alkenes (A) with potassium permanganate was effected in an acetone solution in the cold, the acetone having been previously heated with potassium permanganate itself. Oxidizing the alkene 3,5-dimethyl-5-ethyloctene-3, synthesized by reacting the unsaturated hydrobromide (I) with propylmagnesium bromide, yielded (after the customary processing) an acid with a b.p. of 213-215°, the composition of which was $C_8H_{16}O_2$, to judge from the analysis of its silver salt, thus corresponding to methylethylpropylacetic acid (b.p. 215-220° [9].)

0.1161 g substance: 0.0502 g Ag. Found %: Ag 43.30. $C_8H_{15}O_2Ag$. Calculated %: Ag 43.01.

Oxidizing the 3,5-dimethyl-5-ethylnonene-3 synthesized by reacting the unsaturated hydrobromide with butylmagnesium bromide yielded an acid, whose silver salt proved upon analysis to be a salt of methylethylbutylacetic acid.

1.1078 g substance: 0.0450 g Ag. Found %: Ag 41.07. $C_9H_{17}O_2Ag$. Calculated %: Ag 40.70.

The oxidation results confirmed the structure of the two hydrocarbons as 3,5-dimethyl-5-ethyloctene-3 and 3,5-dimethyl-5-ethylnonene-3, respectively.

Bromination of the alkenes (A) was effected in a chilled ether solution and was accompanied by the evolution of considerable hydrogen bromide. After the bromination products had received the usual treatment, they were vacuum-distilled in a current of nitrogen. The constants of the synthesized unsaturated monobromides (III), apparently of the vinyl type, are listed in Table 2. The monobromides darkened considerably upon standing.

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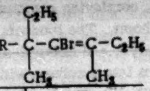
* In every case, the initial mixture of dienes was recovered as a low-boiling distillation fraction (b.p. 135-145°), constituting 30-40% of the dienes (b.p. 136-142° [1]) used for the hydrobromination reaction. Thus, the reaction of the unsaturated tertiary bromide (I) with organomagnesium compounds involved the splitting out of hydrogen bromide from it.

TABLE 2

Unsaturated Monobromides of the General Structure



$$R-\overset{C_2H_5}{\underset{CH_3}{C}}-CBr=\underset{CH_3}{C}-C_2H_5$$

Where R is	B.p.	n_D^{20}	d_4^{20}	MR$_D$	
				Found*	Calc.
C_3H_7	93-95° (12 mm)	1.4808	1.0909	64.47	64.91
iso-C_3H_7	89-90 (4 mm)	1.4917	1.0970	65.46	64.91
C_4H_9	102-104 (2 mm)	1.4860	1.0748	69.75	69.56
iso-C_4H_9	94-95 (3 mm)	1.4830	1.0590	70.46	69.56

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* The substantial discrepancies (0.4-0.9) between the experimental molecular refractions of the monobromides and the calculated values may be due to traces of the respective dibromides; whenever we distilled the bromination products of the alkenes, we secured high-boiling fractions that contained a mixture of unsaturated monobromides and dibromides.

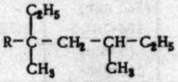
Analysis of the bromination product of 3,5-dimethyl-5-ethyloctene-3 confirmed that its structure was that of the unsaturated monobromide 4-bromo-3,5-dimethyl-5-ethyloctene-3.

8.80 mg substance: 7.56 mg H_2O; 18.80 mg CO_2; 2.86 mg Br_2. 10.31 mg substance; 8.61 mg H_2O; 22.04 mg CO_2; 3.38 mg Br_2. Found %: C 58.30, 58.34; H 9.61, 9.35; Br 32.6, 32.8. $C_{12}H_{23}Br$. Calculated %: C 58.18; H 9.38; Br 32.35.

Behavior of the synthesized allylbenzene homolog (II) in contact with chromic oxide on alumina. The allylbenzene homolog 3,5-dimethyl-5-phenylheptene-3 (II), synthesized by reacting the unsaturated hydrobromide (I) with phenylmagnesium bromide, was passed over an isomerizing (shifting the double bond) contact agent, consisting of chromic oxide on alumina [3] at 250° in a current of nitrogen. After the resulting catalyzate had been distilled over sodium, its constants were the same as those of the initial hydrocarbon (Table 1): b.p. 255-256° at 752 mm; n_D^{20} 1.5320; d_4^{20} 0.9249. Hence, 3,5-dimethyl-5-phenylheptene-3 underwent no change under the specified conditions, i.e., it did not undergo the conversion into propenylbenzene (and its homologs) that is characteristic of allylbenzene (and its homologs), which proves that the structure of this hydrocarbon contains a quaternary carbon atom located between the double bond and the aromatic nucleus.

TABLE 3

Hydrocarbons of the General Structure



$$R-\overset{C_2H_5}{\underset{CH_3}{C}}-CH_2-\underset{CH_3}{CH}-C_2H_5$$

Where R is	Hydrocarbon	Boiling point	n_D^{20}	d_4^{20}	MR$_D$	
					Found	Calculated
C_3H_7	3,5-Dimethyl-5-ethyloctane............	188.5-189° (750 mm)	1.4315	0.7695	57.23	57.60
iso-C_3H_7......	2,3,5-Trimethyl-3-ethylheptane.......	197.5-198° (759 mm)	1.4387	0.7820	57.25	57.61
C_4H_9...........	3,5-Dimethyl-5-ethylnonane...........	213-214° (760 mm)	1.4356	0.7761	62.06	62.23
iso-C_4H_9.....	2,4,6-Trimethyl-4-ethyloctane........	79-80° (7 mm)	1.4349	0.7760	61.98	62.23
C_6H_{11}..........	3,5-Dimethyl-5-cyclohexylheptane..	98-99° (2 mm)	1.4679	0.8515	68.73	69.27

Catalytic hydrogenation of the alkenes (A) and of the homolog of allylcyclohexane (R = C_3H_7, iso-C_3H_7, C_4H_9, iso-C_4H_9, and C_6H_{11}) was effected at 170° over platinized charcoal (15% Pt). The catalyzates did not decolorize bromine water or an aqueous solution of potassium permanganate. The resultant alkanes, containing a quaternary carbon atom, were distilled over sodium into a column with an efficiency of 25 theoretical trays, while the cyclohexane hydrocarbon (with a quaternary carbon atom in the side chain) was distilled in vacuo. The constants of all these hydrocarbons (A') are listed in Table 3, their analysis data being found in Table 4.

When we investigated the Raman spectra* of the synthesized alkanes, we found more or less intense frequencies in the ~1200 cm^{-1} region, an indication (according to B. I. Stepanov [5]) that the hydrocarbon molecule contains a quaternary carbon atom, which agrees satisfactorily with the values of the fully symmetrical frequencies present in the spectra in the ~700 cm^{-1} region [10]. Thus, the spectrum of 3,5-dimethyl-5-ethyloctane (R = = C_3H_7) [10] exhibited the frequencies 1200(2), 1213(1.5), and 1249(1), as well as the fully symmetrical frequency 728(6; b); the spectrum of 2,3,5-trimethyl-3-ethylheptane (R = iso-C_3H_7) exhibiting the frequency 1219(2.5) and

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* We are indebted to V. M. Tatevsky and E. G. Treshchova for having carried out the optical investigations.

TABLE 4

	Hydrocarbon	mg substance	mg CO_2	mg H_2O	Found % C	Found % H	Calculated % C	Calculated % H	General Formula
Alkenes	3,5-Dimethyl-5-ethyloctene-3	5.540	17.112	6.952	85.63	14.23	85.63	14.37	$C_{12}H_{24}$
		6.590	20.682	8.497	85.59	14.43			
	3,5,6-Trimethyl-5-ethylheptene-3	7.020	22.020	8.995	85.55	14.34	85.63	14.37	$C_{12}H_{24}$
		6.710	21.050	8.560	85.57	14.28			
	3,5-Dimethyl-5-ethylnonene-3	5.915	18.570	7.605	85.62	14.39	85.62	14.38	$C_{13}H_{26}$
		4.385	13.760	5.625	85.58	14.36			
	3,5,7-Trimethyl-5-ethyloctene-3	2.860	8.980	3.670	85.63	14.36	85.62	14.38	$C_{13}H_{26}$
		5.020	15.760	6.450	85.62	14.38			
Alkanes	3,5-Dimethyl-5-ethyloctane	7.105	22.077	9.742	84.76	15.34	84.62	15.38	$C_{12}H_{26}$
		3.955	12.274	5.397	84.64	15.27			
	2,3,5-Trimethyl-3-ethylheptane	4.800	14.872	6.609	84.50	15.30	84.62	15.38	$C_{12}H_{26}$
		4.670	14.477	6.422	84.55	15.28			
	3,5-Dimethyl-5-ethylnonane	5.860	18.15	9.818	84.52	15.46	84.69	15.31	$C_{13}H_{28}$
		8.220	25.42	13.70	84.60	15.40			
	2,4,6-Trimethyl-4-ethyloctane	4.375	13.577	6.004	84.64	15.25	84.69	15.31	$C_{13}H_{28}$
		4.464	13.871	6.098	84.75	15.18			

the fully symmetrical frequency 692(10); and the spectrum of 3,5-dimethyl-5-ethylnonane (R = C_4H_9) exhibiting the frequency 1200(2; b) and the fully symmetrical frequency 732(3;b).

SUMMARY

1. A series of alkenes containing a quaternary carbon atom: 3,5-dimethyl-5-ethyloctene-3; 3,5,6-trimethyl-5-ethylheptene-3; 3,5-dimethyl-5-ethylnonene-3; and 3,5,7-trimethyl-5-ethyloctene-3, as well as aromatic and cyclohexane hydrocarbons with a quaternary carbon atom in a side chain: 3,5-dimethyl-5-phenylheptene-3 and 3,5-dimethyl-5-cyclohexylheptene-3, has been synthesized by reacting an unsaturated tertiary bromide of the allylic type, 5-bromo-3,5-dimethylheptene-3, with organomagnesium compounds (RMgHal, where R = C_3H_7, iso-C_3H_7, C_4H_9, iso-C_4H_9, C_6H_5, and C_6H_{11}).

2. The presence of a quaternary carbon atom in the synthesized unsaturated hydrocarbons, located between the double bond and the radical R, has been established by analyzing the oxidation products of two hydrocarbons: 3,5-dimethyl-5-ethyloctene-3 and 3,5-dimethyl-5-ethylnonene-3 (R = C_3H_7 and C_4H_9) and by the passivity of 3,5-dimethyl-5-phenylheptene-3 (R = C_6H_5), a homolog of allylbenzene, when in contact with chromic oxide on alumina.

3. The structure of the synthesized unsaturated hydrocarbons as trisubstituted ethylenes (i.e., the presence of the $-CH=C<$ group in them) has been established by the production, during bromination, of unsaturated monobromides of the vinyl type, formed by the splitting out of hydrogen bromide from the normal bromination products – secondary-tertiary dibromides.

4. Several alkanes with a quaternary carbon atom: 3,5-dimethyl-5-ethyloctane; 2,3,5-trimethyl-3-ethylheptane; 3,5-dimethyl-5-ethylnonane; and 2,4,6-trimethyl-4-ethyloctane, as well as a cyclohexane hydrocarbon with a quaternary carbon atom in the side chain: 3,5-dimethyl-3-cyclohexylheptane, were produced by catalytically hydrogenating the synthesized unsaturated hydrocarbons.

5. The presence of a quaternary carbon atom in the synthesized alkanes has been confirmed by analysis of their Raman spectra.

6. The 11 hydrocarbons synthesized in the present research have not been described in the literature.

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Received July 19, 1950

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SYNTHESIS OF HYDROCARBONS

XXII. THE CONVERSION OF DIENES INTO CYCLOPROPANES

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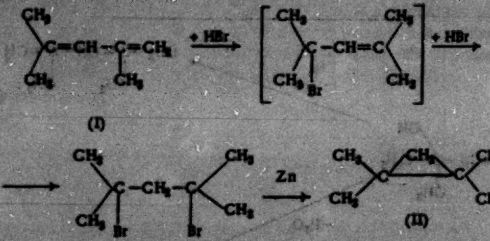
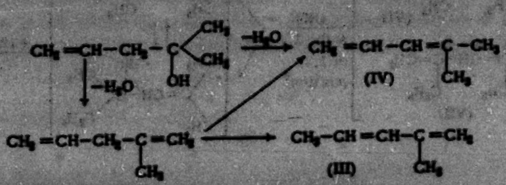
In one of our previous reports [1] we described a new method of producing a cyclopropane with two quaternary carbon atoms – producing 1,1,2,2-tetramethylcyclopropane (II) from an asymmetrical diene of the conjugated type: 2,4-dimethylpentadiene-1,3 (I):



In the present research we have shown that other dienes containing conjugated double bonds, whose structure is a branched one, can also be converted into the respective cyclopropanes by adding two molecules of hydrogen bromide (giving rise to 1,3-dibromides) and splitting two atoms of bromine from the latter by means of zinc dust (Gustavson reaction [2]).

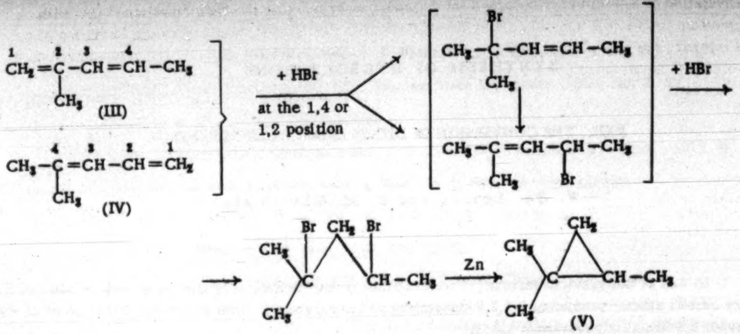
The initial branched dienes were produced by dehydrating unsaturated tertiary alcohols – dimethylallylcarbinol, 2,4-dimethylhexen-2-ol-4, and 3,5-dimethylhepten-3-ol.

Dehydration of dimethylallylcarbinol was effected by passing it over chromic oxide on alumina, employing the method developed previously by one of the present authors [3], which furnishes a high yield of a mixture of isomeric conjugated C_6H_{10} dienes — 2-methylpentadiene-1,3 (III) and 4-methylpentadiene-1,3 (IV):

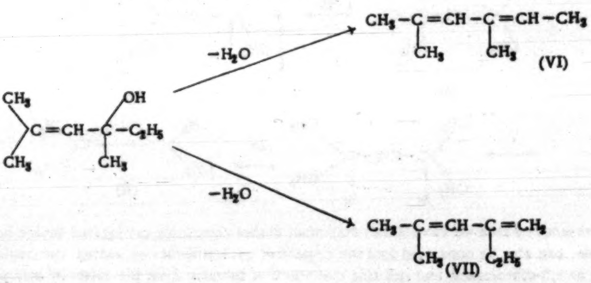


Adding the first molecule of hydrogen bromide to the mixture of these conjugated dienes at the 1,4 and 1,2 positions results in the formation of an allylic bromide, which can then react further in two isomeric forms, related by allyl rearrangement [4]; adding the second molecule of hydrogen bromide yields a 1,3-dibromide, the reaction of which with zinc dust yields 1,1,2-trimethylcyclopropane (V): (see (A) following page).

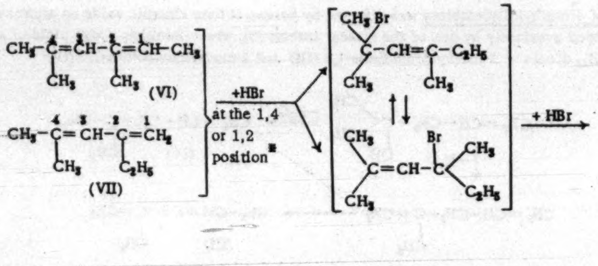
Dehydration of 2,4-dimethylhexen-2-ol-4 (produced by reacting mesityl oxide with ethylmagnesium bromide) was effected by simply distilling it, resulting in the production of a mixture of isomeric conjugated C_8H_{14} dienes with the same carbon skeleton – 2,4-dimethylhexadiene-2,4 (VI) and 2-ethyl-4-methylpentadiene-1,3 (VII) [5]:



(A)



The addition of two molecules of hydrogen bromide to the resulting mixture of dienes yielded a 1,3-dibromide, the reaction of which with zinc dust yielding 1,1,2-trimethyl-2-ethylcyclopropane (VIII):



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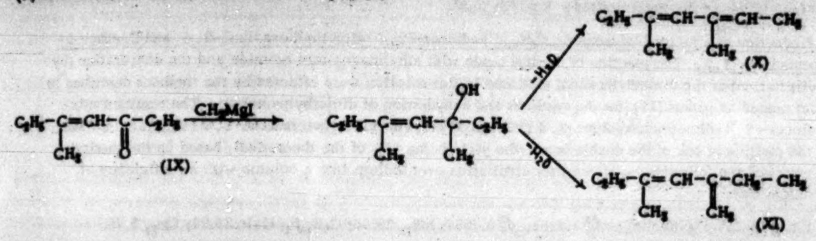
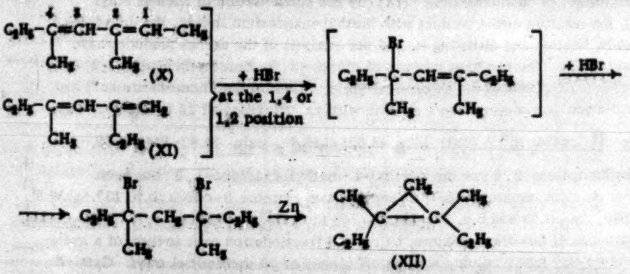
[*] The addition of the first molecule of hydrogen bromide at the 3,4 position to these conjugated branched dienes would have resulted in the formation of monobromides that were not of the allylic type, such monobromides not having been detected in any of the cases described in the literature.

Dehydration of 3,5-dimethylhepten-3-ol-5 (produced by reacting the "homomesitone" (IX) with methylmagnesium iodide [8]) was effected by heating and then distilling it, resulting in the formation of a mixture of isomeric conjugated C_9H_{16} dienes with the same carbon structure—3,5-dimethylheptadiene-2,4 (X) and 2-ethyl-4-methylhexadiene-1,3 (XI) [7]:

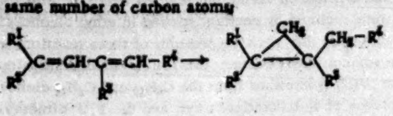


Adding a single molecule of hydrogen bromide to a mixture of these dienes at the 1,2 or 1,4 position results in the formation of an allylic unsaturated tertiary bromide, which exists in only one form (no allylic rearrangement taking place) [6]; the addition of more hydrogen bromide to this hydrobromide resulted in the formation of a 1,3-dibromide, whose reaction with zinc dust yielded a cyclopropane with two quaternary carbon atoms—1,2-dimethyl-1,2-diethylcyclopropane (XII), not described in the literature:



Study of the cyclization of ditertiary 1,3-dibromides, carried out for the first time in our previous and present papers, has convincingly shown that the Gustavson reaction (the action of zinc dust upon 1,3-dibromides) can be successfully employed with ditertiary dibromides, contrary to the opinion of Shortridge and Boord [9], these dibromides being transformed with good yields (50-80%) into cyclopropanes with two quaternary carbon atoms.

The results of the present research have likewise finally established the general nature of the new reaction we have proposed for the direct conversion of aliphatic branched conjugated dienes into homologs of cyclopropane with the same number of carbon atoms:



(where all the R's denote radicals or else one or two of them are hydrogen atoms).

EXPERIMENTAL

Production of a mixture of isomeric C_6H_{10} alkadienes—2-methylpentadiene-1,3 and 4-methylpentadiene-1,3. The procedure involved in the synthesis of dimethylallylcarbinol (67-70% of the theoretical yield), its catalytic dehydration over chromic oxide on alumina at 250°, and the analysis of the resultant dienes have been described in one of our preceding papers [3]. The synthesizing mixture of 2-methylpentadiene-1,3 (III) and 4-methylpentadiene-1,3 (IV) (59% of the theoretical yield) was distilled over sodium into a column with an efficiency of 25 theoretical trays, after which its constants were as follows:

B.p. 72.5-75.5° (761 mm); n_D^{20} 1.4474; d_4^{20} 0.7147; MR_D 30.69; $C_6H_{10}F_2$: calculated 28.97; EM_D 1.72.

Figure given in the literature [10]: B.p. 73-75.8°.

Production of a mixture of isomeric C_8H_{14} alkadienes—2,4-dimethylhexadiene-2,4 and 2-ethyl-4-methylpentadiene-1,3. The reaction of mesityl oxide with ethylmagnesium bromide and the dehydration (by simple distillation) of the dimethylhexenol produced in this reaction were effected by the methods described in one of our preceding papers [11] (for the synthesis and dehydration of dimethylpentenol). The resultant mixture of dienes—2,4-dimethylhexadiene-2,4 (VI) and 2-ethyl-4-methylpentadiene-1,3 (VII), which differ only in the position of one of the double bonds (the yield being 60% of the theoretical, based on the mesityl oxide), possessed the following constants after distillation over sodium into a column with an efficiency of 25 theoretical trays:

B.p. 114-117.5° (760 mm); n_D^{20} 1.4461; d_4^{20} 0.7537; MR_D 39.00; $C_8H_{14}F_2$; Calc. 38.21; EM_D 0.79.

Figures given in the literature [12] for the individual components of this mixture of dienes, separated by distillation: 2,4-dimethylhexadiene-2,4—b.p. 116° (752 mm) n_D^{22} 1.4540, d_4^{22} 0.7663; 2-ethyl-4-methylpentadiene-1,3—b.p. 113-113.5° (752 mm) $n_D^{18.8}$ 1.4444, $d_4^{18.8}$ 0.7660.

Production of a mixture of isomeric C_9H_{16} alkadienes—3,5-dimethylheptadiene-2,4 and 2-ethyl-4-methylhexadiene-1,3. The synthesis of "homomesitone" (IX) (by the condensation of methyl ethyl ketone, using calcium carbide), the reaction of the product with methyl-magnesium iodide, the dehydration of the resultant dimethylheptenol by heating and distilling it, and the analysis of the dienes produced have been described in preceding reports [6,7]. The resultant mixture of dienes—3,5-dimethylheptadiene-2,4(X) and 2-ethyl-4-methylhexadiene-1,3 (XI) (86% of the theoretical yield, based on the "homomesitone") had the following constants after distillation over sodium into a column with an efficiency of 25 theoretical trays:

B.p. 136-142° (760 mm); n_D^{20} 1.4474; d_4^{20} 0.7631; MR_D 43.52; $C_9H_{16}F_2$; calc. 42.83; EM_D 0.69.

Neither the 3,5-dimethylheptadiene-2,4 nor the 2-ethyl-4-methylhexadiene-1,3 has been described in the literature. In our previous researches [6,7] we secured two extreme fractions (b.p. 137.4-137.6° at 766 mm; n_D^{20} 1.4490, d_4^{20} 0.7645, EM_D 0.75 and b.p. 141-141.4° (740 mm), n_D^{20} 1.4522, d_4^{20} 0.7673, EM_D 0.86), representing the two stated constituents of this diene mixture, by careful fractionation over sodium of a hydrocarbon mixture produced in the same way into a column with an efficiency of 40 theoretical trays. Catalytic hydrogenation [7] of both the diene mixture (b.p. 136-142°) and the specified fractions thereof yielded the same alkane—3,5-dimethylheptane, proving that their carbon skeletons were identical.

Producing cyclopropanes from dienes. Hydrogen bromide, dried and freed of all traces of bromine, was passed through each diene mixture (C_6H_{10}, C_8H_{14}, and C_9H_{16}), chilled to -5° until saturation was complete. Two molecules of hydrogen bromide were added to 10 g of the dienes within 40-50 minutes (90-92% of the calculated quantity of hydrogen bromide being absorbed). The resultant dihydrobromides (1,3-dibromides, one secondary-tertiary and the other two ditertiary) were not isolated in the individual state, inasmuch as hydrogen bromide was split off when they were heated and distilled in vacuo, but reacted with zinc dust immediately after they had been produced. The dibromides were cyclized by constant stirring in ethyl alcohol (96%) with four times their weight of zinc dust. The cyclopropanes that were the products of these reactions were processed in the usual manner and then distilled over sodium into a column, the 1,1,2-trimethylcyclopropane (V) and the 1,1,2-trimethyl-2-ethylcyclopropane (VIII) synthesized from the C_6H_{10} and C_8H_{14} dienes, respectively, being distilled into a column with an efficiency of 40 theoretical trays, and the 1,2-dimethyl-1,2-diethylcyclopropane (XII) synthesized from the C_9H_{16} dienes being distilled into a column with an efficiency of 50 theoretical trays.

These cyclopropanes did not decolorize a solution of potassium permanganate and decolorized a solution of bromine in carbon tetrachloride very slowly. They exhibited the exaltation of the molecular refraction (0.72-0.98) characteristic of hydrocarbons containing a three-membered ring [1,8]. The constants and yields of the cyclopropanes are given in Table 1, their analyses being set forth in Table 2. Analysis of their Raman spectra indicated that the trimethylcyclopropane (V) and the dimethyldiethylcyclopropane (XII) contained no traces of ethylenic or diene hydrocarbons, while the trimethylethylcyclopropane (VIII) contained a small quantity (up to 5%) of a hydrocarbon having a double bond.

TABLE 1

Cyclopropanes	B.p.	n_D^{20}	d_4^{20}	MR_D		EM_D	Aniline point	Found	
				Found	Calc.			g.	% of theoretical, based on initial diene mixture
1,1,2-Trimethylcyclopropane	52.0-52.3° (760 mm)	1.3845	0.6861	28.68	27.70	0.98	47.2°	42	84
1,1,2-Trimethyl-2-ethylcyclopropane	103.6-104 (754 mm)	1.4160	0.7408	37.92	36.94	0.98	51.0	22	80
1,2-Dimethyl-1,2-diethylcyclopropane *	131.1-131.3 (768 mm)	1.4230	0.7595	42.28	41.56	0.72	58.0	48	81

* This hydrocarbon, not described in the literature, can exist in two stereoisomeric (cis and trans) forms whose boiling points are closer together. When 56 g of this hydrocarbon was distilled into a column with an efficiency of 50 theoretical trays, we secured 48 g of a fraction with b.p. of 131.1-131.3°, the remainder boiling up to 132.9°.

Data in the Literature:

1,1,2-Trimethylcyclopropane—b.p. 56-57° (750 mm); n_D^{195} 13.848; $d_4^{19\ 5}$ 0.6822; MR_D 28.81; EM_D 1.10 [13]; b.p. 52.1° (736 mm); n_D^{20} 1.3850; d_4^{20} 0.6853; MR_D 28.78; EM_D 1.08 [14].

1,1,2-Trimethyl-2-ethylcyclopropane—b.p. 103.5-104.5°; n_D^{204} 1.4129; d_4^{204} 0.7418; MR_D 37.69; EM_D 0.75 [15].

TABLE 2

Hydrocarbon	Wt, mg	CO_2, mg	H_2O, mg	Found (%)		Calculated %		General formula
				C	H	C	H	
1,1,2-Trimethylcyclopropane . .	4.120 4.840	12.920 15.210	5.290 6.207	85.53 85.71	14.37 14.35	85.63	14.37	C_6H_{12}
1,1,2-Trimethyl-2-ethylcyclopropane	3.290 4.630	10.320 14.520	4.240 5.960	85.62 85.58	14.42 14.41	85.62	14.38	C_8H_{16}
1,2-Dimethyl-1,2-diethylcyclopropane	7.100 6.120	22.310 19.230	9.130 7.880	85.71 85.70	14.39 14.30	85.63	14.37	C_9H_{18}

SUMMARY

1. The method we have developed for synthesizing cyclopropanes from conjugated dienes of iso structure (by adding two molecules of hydrogen bromide to the latter and then splitting bromine out of the resulting 1,3-dibromides by means of zinc dust) has been utilized to synthesize three homologs of cyclopropane containing one or two quaternary carbon atoms.

2. 1,1,2-Trimethylcyclopropane, 1,1,2-trimethyl-2-ethylcyclopropane, and 1,2-dimethyl-1,2-diethylcyclopropane (not described in the literature) have been synthesized in this manner, the respective yields being 61, 56, and 81% of the theoretical, based on the initial dienes.

3. The opinion of American chemists that ditertiary 1,3-dibromides cannot be cyclized in a Gustavson reaction has been disproved.

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Received July 19, 1950

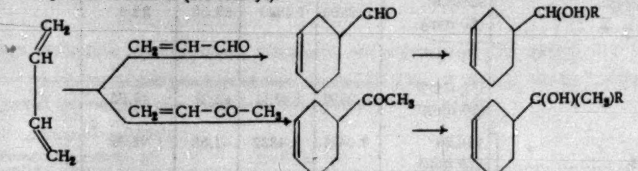
Moscow State University,
Awarded the Order of Lenin.

THE SYNTHESIS AND PROPERTIES OF SOME ISOMERS, HOMOLOGS, AND ANALOGS OF α-TERPINEOL BASED ON 1,3-DIENES

A.A.Petrov and N.P.Sopov

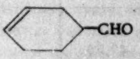
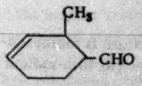
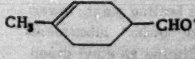
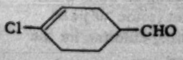
In earlier papers [1-3] the authors of this article investigated for the first time the condensation of 1,3-diene compounds with α,β-unsaturated ketones, which results in the synthesis of hydroaromatic ketones. These syntheses opened up a convenient transition from dienes to hydroaromatic alcohols of the α-terpineol type. This method had not been discussed in the literature prior to that time, though there were isolated references to the production of secondary hydroaromatic alcohols from dienes. Ethyl-(2,5-dimethylcyclohexen-3-yl)-carbinol was synthesized, for example, by reacting C_2H_5MgI with the condensation product of hexadiene-2,4 and crotonaldehyde [4], while several bicyclic alcohols were synthesized by reacting organomagnesium compounds with the condensation products of cyclohexadiene and cyclopentadiene with acrolein [5,6]. Inasmuch as only very few secondary hydroaromatic alcohols have been synthesized by this method, we included this synthesis in our research program.

The present paper describes the synthesis of secondary and tertiary hydroaromatic alcohols from 1,3-diene compounds as follows (for divinyl):

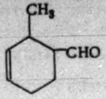


All the hydroaromatic aldehydes synthesized by us for this research have already been described in the literature. The condensation product of divinyl and acrolein, formylcyclohexene-3, has been described in detail by Chayanov [7]. 2-Methylformylcyclohexene-3 was first described by B.A.Arbuzov and his associates [4]. The constants of the aldehydes we used in our research are compared in Table 1 with the figures given in the literature.

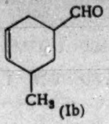
TABLE 1

Substance	B.p.	d_4^{20}	n_D^{20}	MR_D Found	MR_D Calc.	Reference
	58-58.5° (20 mm)	0.9725	1.4732	31.78	31.87	[7]
	52-53 (12 mm)	0.9650	1.4725	31.99	31.87	
	70.5-71 (20 mm)	0.9528	1.4715	36.45	36.49	[8]
	56-58 (11 mm)	0.9435	1.4653	36.35	36.49	
	73.5-74.5 (20 mm)	0.9490	1.4732	36.72	36.49	[6,10]
	64-66 (12 mm)	0.9630 (at 13°)	–	–	–	
	104-104.5 (20 mm)	1.1589	1.5033	36.89	36.73	[3]

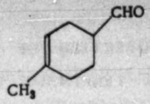
Condensation of acrolein with piperylene and isoprene might be expected to yield two products in each case:



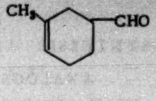
(Ia)



(Ib)



(IIa)



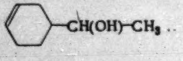
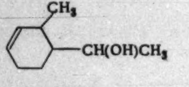
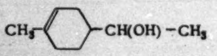
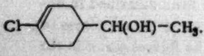
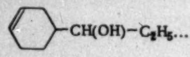
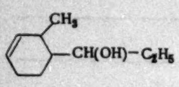
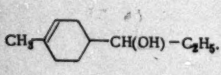
(IIb)

The structure of the aldehyde synthesized from acrolein and piperylene was first established by one of the present authors by oxidizing it to 2-methylcyclohexene-3-carboxylic acid with a chromic acid mixture [9]. The same acid was secured in crystalline form by oxidizing this aldehyde with moist silver oxide [8]. This proved that the substance had an "ortho" structure (Ia).

We established the structure of the condensation product of acrolein and isoprene by oxidizing it with moist silver oxide to crystalline 4-methylcyclohexene-3-carboxylic acid.

The structure of the aldehyde synthesized from chloroprene was not established, though there is every reason to believe that it has a "para" structure [3].

TABLE 2

Substance	Boiling point	d_4^{20}	n_D^{20}	MR_D		Reference
				Found	Calculated	
	93-93.5° (20 mm)	0.9592	1.4842	38.53	38.0	
	102-102.5° (20 mm)	0.9492	1.4834	42.21	42.62	
	106.25 (20 mm)	0.9421	1.4832	42.53	42.62	
	212-213° (760 mm)	0.942 (at 19°)	1.4836 (at 19°)	42.55	42.62	[11]
	124.5° (20 mm)	1.1194	1.5060	42.65	42.84	
	104-104.5 (20 mm)	0.9503	1.4832	42.16	42.62	
	111.5-112 (20 mm)	0.9406	1.4830	46.83	47.24	
	116.5-117° (20 mm)	0.9374	1.4828	46.98	47.24	

The only one of the secondary alcohols we synthesized that is described in the literature is methyl-(4-methylcyclohexen-3-yl)-carbinol. It was synthesized by reducing 4-methylacetylcyclohexene-(3) with sodium in alcohol [11].

The following conclusions may be drawn from a comparison of the constants of the substances listed in the table. Introducing a methyl group into the first compound listed in the table raises its boiling point, lowers its specific gravity, and has but little influence upon its refractive index. Compounds with "ortho" substituents have a lower boiling point and a higher specific gravity than "para" compounds. Substituting an ethyl group for the methyl group in the side chain (attached to the alcohol group) raises the boiling point (some 10°) and lowers the specific gravity, the change in the refractive index being insignificant. Substituting chlorine for the methyl group raises the boiling point, the specific gravity, and the refractive index considerably. All the secondary alcohols we synthesized were fragrant. The alcohols that had no methyl group attached to the ring had an alcoholic odor. The alcohols in which the methyl group was in the "ortho" position had a sweetish odor. The alcohols with an ethyl group in the side chain had various shades of a mint odor. Methyl-(4-methylcyclohexen-3-yl)-carbinol had an odor that resembled that of α-terpineol (flower fragrance) most closely.

Of the chemical properties of the synthesized secondary alcohols, we investigated their behavior in the presence of bromine and in acetylation and oxidation. We were unable to secure crystalline substances by the action of bromine. Acetylation with acetic anhydride yielded three acetates, the constants of which are given in Table 3.

TABLE 3

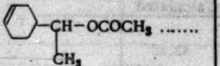
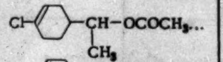
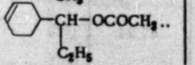
Formula	B.p. at 20 mm	d_4^{20}	n_D^{20}	MR_D	
				Found	Calc.
	101-101.5°	0.9777	1.4594	47.08	47.37
	137.5-138°	1.1050	1.4806	52.27	52.24
	113.5-114	0.9668	1.4608	51.70	51.99

Table 3 shows that the acetates have higher boiling points, higher specific gravities, and much lower refractive indexes than the alcohols. The odor of the acetates is fragrant and strong.

Oxidizing the secondary alcohols with a chromic acid mixture yields hydroaromatic ketones that are the same as those obtainable by condensing the respective dienes with methyl vinyl ketone.

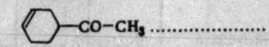
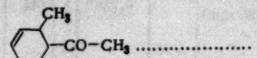
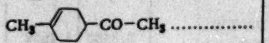
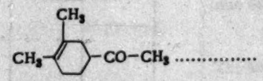
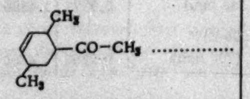
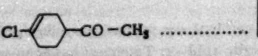
We secured tertiary alcohols by using the hydroaromatic ketones produced by condensing divinyl, piperylene, diisopropenyl, dipropenyl, and chloroprene with methyl vinyl ketone.

The formulas and constants of these ketones are given in Table 4. All these ketones, with the exception of the second and the fifth ones, have been described in previous papers.

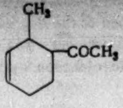
The structure of the condensation products of methyl vinyl ketone and the symmetrical dienes is not subect to any doubt. We might expect two isomeric hydroaromatic ketones to be formed when methyl vinyl ketone is condensed with piperylene and isoprene: (see following page).

The choice of the first (IIIa) and third (IVa) formulas, respectively, for these ketones was based upon the fact that the substance isolated proved to be the same as the ketones produced by oxidizing methyl-(2-methylcyclohexen-3-yl)- and methyl-(4-methylcyclohexen-3-yl)-carbinols, the structures of which have been established beyond any doubt.

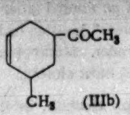
TABLE 4

Formula	B.p. at 20 mm	d_4^{20}	n_D^{20}	MR_D	
				Found	Calc.
	77.5-78.5°	0.9580	1.4698	36.15	36.49
	85-86	0.9387	1.4682	41.18	41.01
	91-91.5	0.9373	1.4706	40.94	41.01
	106.5-107	0.9374	1.4784	45.64	45.62
	100-102	0.9359	1.4732	45.72	45.62
	120-120.5	1.1216	1.4972	41.38	41.35

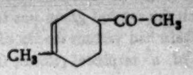
The structure of the condensation product of methyl vinyl ketone and chloroprene has not been established, though we may confidently assign it the formula given in the table, since alkyl vinyl ketones usually yield "para" products when reacted with chloroprene [12].



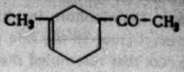
(IIIa)



(IIIb)



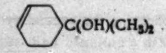
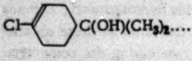
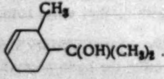
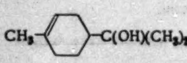
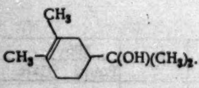
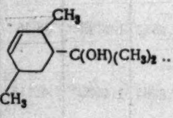
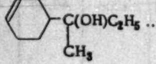
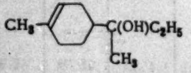
(IVa)



(IVb)

The reaction of CH_3MgI and C_2H_5MgI under the usual conditions with the ketones listed in the table yielded α-terpineol and several of its isomers, homologs, and analogs. The constants of the substances synthesized are collated in Table 5 with the findings of other researchers for these substances, insofar as these figures are to be found in the literature.

TABLE 5

Formula	Boiling point	d_4^{20}	n_D^{20}	MR_D		Reference
				Found	Calculated	
	95.5-96° (20 mm)	0.9479	1.4824	42.21	42.62	
	132-133° (20 mm)	1.0960	1.5038	47.17	47.47	
	102-103° (20 mm)	0.9405	1.4838	46.90	47.24	
	110-112° (30 mm)	0.9404	1.4792	46.53	47.24	[13]
	109.5-110° (20 mm)	0.9344	1.4830	47.17	47.24	
	120-122° (30 mm)	0.9350	1.4831	47.17	47.24	[14]
	121-121.5° (20 mm)	0.9370	1.4882	51.76	51.86	
	111.5-112.5 (20 mm)	0.9367	1.4844	51.30	51.86	
	108-109 (20 mm)	0.9483	1.4852	46.65	47.24	
	120-121° (20 mm)	0.9377	1.4850	51.30	51.86	
	235-237° (760 mm)	0.9390	1.4850	51.28	51.86	[14]

Dimethyl-(2-methylcyclohexen-3-yl)-carbinol was previously synthesized by reacting CH_3MgI with the ethyl ester of 2-methylcyclohexene-3-carboxylic acid. α-Terpineol has been synthesized in many ways, including the action of CH_3MgI upon 4-methylacetylcyclohexene-3 [14].

The action of C_2H_5MgI upon this ketone likewise yielded methylethyl-(4-methylcyclohexen-3-yl)-carbinol [14]. These syntheses were effected by Wallach. Wallach thus had in mind the possibility of synthesizing terpene alcohols from hydroaromatic ketones, but the relative inaccessibility of these ketones at that time did not permit of the extensive utilization of this method. There is practically no difference between the constants of the tertiary alcohols determined by us and by previous research workers.

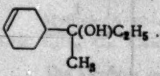
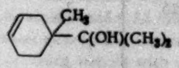
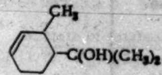
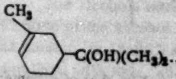
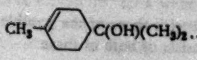
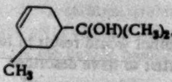
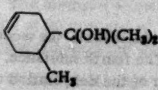
Dimethyl-(3,4-dimethylcyclohexen-3-yl)-carbinol crystallized in storage. The m.p. of this substance was 38-42° before recrystallization.

All the substances listed in Table 5 possess various shades of a flower fragrance.

Our work on the synthesis of tertiary alcohols from the respective ketones has disclosed all the isomers of *a*-terpineol that differ in the position of the methyl group, with the sole exception of dimethyl-(1-methylcyclohexen-3-yl)-carbinol. We secured this last isomer by reacting CH_3MgI with the condensation product of divinyl and a methyl methacrylate – the methyl ester of 1-methylcyclohexene-3-carboxylic acid.

Comparing the properties of all these isomers yields interesting condlusions concerning the change in their properties with a shift in the position of the methyl group. We see from Table 6 that as the radicals apprcach each other the boiling point drops, while the specific gravity and the refractive index increase. The sharp increase in the last two variables in compounds in whose molecules the two radicals are attached to the same carbon atom is worthy of note. The agreement between the experimental and the calculated values of the molecular refraction is best in the compounds with the substituents in the "para" position.

TABLE 6

Formula	Boiling point	d_4^{20}	n_D^{20}	MR_D		Reference
				Found	Calculated	
	108-109° (20 mm)	0.9483	1.4852	46.65	47.24	–
	103.5-104 (20 mm)	0.9619	1.4912	46.46	47.24	–
	102-103 (20 mm)	0.9405	1.4838	46.90	47.24	–
	106-107 (20 mm)	0.9359	1.4775(*a*)	46.61(*a*)	46.99(*a*)	[15]
	109.5-110 (20 mm)	0.9344	1.4830	47.14	47.24	–
	104-105 (20 mm)	–	–	–	–	[16]
	110 (30 mm)	–	–	–	–	[17]

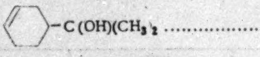
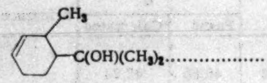
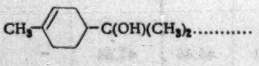
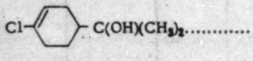
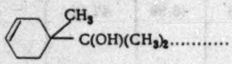
It is also of interest that all the isomers of *a*-terpineol at our disposal had different odors. The odor of the first substance (Table 6) reminds one of the odor of peppermint. The second substance has a strong camphor odor; at higher concentrations the vapor of this substance irritates the mucous membrane of the eye. The odor of the third substance is like that of the fourth – like *a*-terpineol – but is weaker and less pleasant. As we know, *a*-terpineol has a fragrant floral odor (lilac).

We investigated the following chemical properties of the tertiary alcohols we hyd synthesized: the behavior with bromine and acetic anhydride and their dehydration. Bromination of the dimethylcyclohexenylcarbinol yielded crystalline (m.p. 87°) and liquid dibromides. Boiling the dibromide of dimethyl-(2-methylcyclohexen-3-yl)-carbinol in an acetic acid solution yielded o-cymene. Acetic anhydride causes dehydration of the alcohols even in the cold when a drop of H_2SO_4 is present.

We dehydrated the tertiary alcohols in various ways: 1) by heating with acetic anhydride; 2) by distilling over P_2O_5; and 3) by distilling with a 5% solution of oxalic acid.

We did not determine the structure of the hydrocarbons synthesized. Mixtures of the two possible isomers were apparently secured in every case but the last one. The constants of the hydrocarbons are given in Table 7.

TABLE 7

Initial alcohol	Constants of dehydration products					Dehydration method
	Boiling point	d_4^{20}	n_D^{20}	MR_D		
				Found	Calculated	
	151-155° (760 mm)	0.8467	1.4774	40.80	40.63	1
	172-174 (760 mm)	0.8544	1.4785	45.18	45.25	1
	176-177 (760 mm)	0.8498	1.4830	45.78	45.25	1
	94.5-95.5 (20 mm)	1.0169	1.5014	45.95	45.50	2
	63-64 (20 mm)	0.8574	1.4768	44.88	45.25	3

The first and last substances have aromatic odors. The odor of the second substance is like that of dipentene.

When we compare the constants of the hydrocarbons synthesized from α-terpineol with those of the possible dehydration products – dipentene and terpinolene, we may conclude that the substance consists of both of these products, with the first one predominating.

It might be expected that dehydration of dimethyl-(1-methylcyclohexen-3-yl)-carbinol would result in formation of only one substance, namely, 1-methyl-1-isopropenylcyclohexene-3. We are the first to have described this substance.

The products of the dehydration of the tertiary alcohols were dehydrogenated over palladium, the second, third, and fourth of these substances yielding the corresponding aromatic hydrocarbons. The fourth substance, for example, loses its halogen atom in dehydrogenation, yielding cumene. When the product of the dehydration of dimethyl-(1-methylcyclohexen-3-yl)-carbinol is passed over palladium under the same conditions, no hydrogen is split off, which is in conformity with its supposed structure.

EXPERIMENTAL

1. Preparation of the initial hydroaromatic aldehydes and ketones. The dienes were condensed with acrolein and methyl vinyl ketone in open glass ampoules inside a steel autoclave at 120-140°. Heating was continued for 6 hours. The yield of hydroaromatic aldehydes and ketones totaled 75-80% of the initial aldehyde or ketone, as a rule. A considerable excess of piperylene and hexadiene-2,4 was used, since only the trans form of these hydrocarbons enters into the reaction.

The constants of the substances synthesized are listed in Table 1 and 4. It should be noted that the boiling points of the hydroaromatic ketones as published in an earlier paper by one of the present authors are somewhat high (by some 2-3°), evidently due to incorrect readings of the vacuum-meter.

The previously unknown p-nitrophenylhydrazone of the piperylene ketone, with a m.p. of 143-144°, has been prepared.

The condensation product of acrolein and isoprene was oxidized under the following conditions. 6.2 g of the aldehyde was added in small portions, with vigorous agitation, to an aqueous suspension of silver oxide, prepared from 16.9 g of $AgNO_3$. After the mixture had been heated for an hour on a water bath, ammonia was added, the precipitated silver was filtered out, the solution acidulated with H_2SO_4, and the organic acid extracted with ether. Driving off the ether yielded 5.5 g of a crystalline acid, which had a m.p. of 85° after having been washed with petroleum ether (0.5 g loss) and 98° after recrystallization from water; this is the figure for 4-methylcyclohexene-3-carboxylic acid [18]. The mixed melting point of the substance synthesized and known 4-methylcyclohexene-3-carboxylic acid exhibited no change.

2. Synthesis and properties of the secondary alcohols. A solution of 0.2 mole of the hydroaromatic aldehyde in 100 ml of ether was added with chilling and mechanical stirring to a solution of an organomagnesium compound, prepared from 0.2 gram-atom of magnesium and 0.22 mole of methyl or ethyl iodide in 200 ml of absolute ether. After the ether solution had stood for 1 hour and been heated for 1.5 hours, it was poured into a flask containing a solution of ammonium chloride and pieces of ice. The ether solution of the secondary alcohol was dried with calcined Na_2SO_4 and then distilled. The yield of alcohols was 78-82%, based on the aldehyde. The constants of the alcohols synthesized are given in Table 2. We cite the analytical data (Table 8).

Methyl-(4-chlorocyclohexen-3-yl)-carbinol. 0.1587 g substance: 0.1494 g AgCl. Found %: Cl 23.26. $C_8H_{13}OCl$. Calculated %: Cl 22.07.

The alcohols were acetylated as follows: One drop of conc. H_2SO_4 was added to a mixture of 0.1 mole of the alcohol and 0.15 mole of acetic anhydride, after which the mixture was agitated and chilled with a jet of water to keep the temperature from rising above 50°. Then the mixture was diluted with water, the resulting oil being washed with water and a soda solution and then distilled. The constants of the resulting acetates are given in Table 3. We cite the analytical findings (Table 9).

Acetate of methyl-(4-chlorocyclohexen-3 yl)-carbinol. 0.1512 g substance: 0.1084 g AgCl. Found %: Cl 17.72. $C_{10}H_{15}O_2Cl$. Calculated %: Cl 17.49.

The alcohols were oxidized as follows. 0.02 mole of sodium dichromate was added to a solution of 0.05 mole of the alcohol in 30 ml of acetic acid, and then 50% H_2SO_4 was added drop by drop (100% excess) with cooling (to 15-20°) and mechanical stirring. After the reaction was over, the solution was diluted and neutralized with soda, and the ketone was extracted with ether. The ketone remaining after the ether had been driven off on a water bath was converted into a semicarbazone (to separate it from the unreacted alcohol) and then recovered from the semicarbazone, washed on the filter with ether, by distillation with a 5% solution of H_2SO_4. The yields of the pure ketone averaged 20-30%. In this way methyl-(2-methylcyclohexen-3-yl)-carbinol yielded 2-methylacetylcyclohexene-3, with a b.p. 85-86° at 20 mm; n_D^{20} 1.4688. The melting point of the p-nitrophenylhydrazone was 142-144°. All these figures correspond exactly with those found for the ketone produced by condensing piperylene with methyl vinyl ketone.

The methyl-(4-methylcyclohexen-3-yl)-carbinol yielded 4-methylacetylcyclohexene-3 with a b.p. of 90-92° at 20 mm and n_D^{20} 1.4710. The melting point of the semicarbazone was 150-151°, and that of the p-nitrophenylhydrazone was 166-167°, which again agrees with the figures given in the literature.

Oxidation of ethyl-(cyclohexen-3-yl)-carbinol yielded the hitherto unknown propionylcyclohexene-3. B.p. 90-90.5° at 20 mm, d_4^{20} 0.9405, n_D^{20} 1.4700, MR_D 40.97. $C_9H_{14}O$F; calculated 41.11.

0.1384 g substance: 0.3957 g CO_2; 0.1284 g H_2O. Found %: C 78.02; H 10.38. $C_9H_{14}O$. Calculated %: C 78.21; H 10.21.

It was difficult to form the semicarbazone of this ketone (precipitation took 3 days). M.p. 138°. It was recrystallized from aqueous alcohol.

We were unable to secure crystalline products by adding nitrosyl chloride to the first and third substances (Table 3) under ordinary conditions.

The alcohols were brominated in a chilled chloroform solution with a calculated quantity of a chloroform solution of bromine. The solvent was driven off in vacuo at room temperature. The first, second, third, and fifth substances (Table 3) were brominated. In every instance we secured a thick oil, which was not analyzed further.

TABLE 8

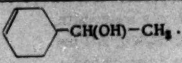
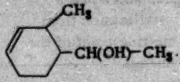
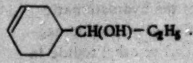
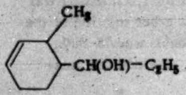
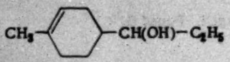
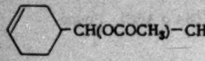
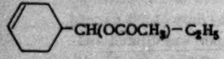
Substance	g	CO_2 g	H_2O g	Found % C	Found % H	Formula	Calculated % C	Calculated % H
	0.1713	0.4816	0.1701	76.72	11.11	$C_8H_{14}O$	76.13	11.18
	0.1687	0.4781	0.1752	77.33	11.62	$C_9H_{16}O$	77.08	11.50
	0.1379	0.3901	0.1355	77.20	11.50	$C_9H_{16}O$	77.08	11.50
	0.1733	0.4958	0.1786	78.07	11.53	$C_{10}H_{18}O$	77.86	11.76
	0.1641	0.4694	0.1634	78.06	11.14	$C_{10}H_{18}O$	77.86	11.76

TABLE 9

Substance	g	CO_2 g	H_2O g	Found % C	Found % H	Formula	Calculated % C	Calculated % H
	0.1546	0.4010	0.1313	70.78	9.28	$C_{10}H_{16}O_2$	71.39	9.58
	0.1342	0.3553	0.1186	72.25	9.88	$C_{11}H_{18}O_2$	72.10	9.90

3. Synthesis and properties of the tertiary alcohols. The tertiary alcohols were synthesized under the same conditions as those used for the secondary alcohols, the yields being somewhat lower in this case: 60-70%.

A tertiary alcohol with two radicals attached to the same carbon atom was synthesized by reacting CH_3MgI in ether with the condensation product of divinyl and methyl methacrylate, which was described in one of our preceding reports [19]. The yield was 89%.

The constants of the tertiary alcohols are given in Table 5. We give below the analytical findings for the substance synthesized for the first time (Table 10).

Bromination of the first and fourth substances listed in Table 5 under the conditions specified in the preceding section yielded viscous oils. Crystals with a m.p. of 87° settled out when the dibromide of the first substance was allowed to stand for a long time. (Found %: Br 53.78).

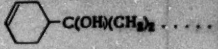
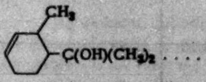
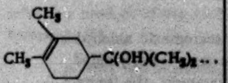
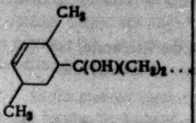
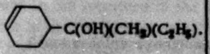
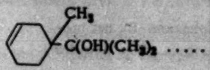
The action of nitrosyl chloride upon α-terpineol yielded a crystalline product with a m.p. of 103°, described in the literature.

Dimethyl-(4-chlorocyclohexen-3-yl)-carbinol. 0.1440 g substance: 0.1206 g AgCl. Found %: Cl 20.72. $C_9H_{15}OCl$. Calculated %: Cl 20.30.

Dimethyl-(cyclohexen-3-yl)-carbinol does not yield a crystalline product whenreacted with nitrosyl chloride.

3.6 g of dimethyl-(2-methylcyclohexen-3-yl)-carbinol was brominated (4 g of bromine in 25 ml of acetic acid). After the solution had boiled for 6 hours (until no more hydrogen bromide was evolved), it

TABLE 10

Substance	g	CO_2 g	H_2O g	Found % C	Found % H	Formula	Calculated % C	Calculated % H
	0.1908	0.5375	0.1916	76.88	11.24	$C_9H_{16}O$	77.08	11.50
	0.1871	0.5321	0.1935	77.61	11.57	$C_{10}H_{18}O$	77.86	11.76
	0.1657	0.4751	0.1674	78.25	11.31	$C_{11}H_{20}O$	78.51	11.98
	0.1453	0.4157	0.1379	78.08	10.64	$C_{11}H_{20}O$	78.51	11.98
	0.1618	0.4617	0.1703	77.87	11.78	$C_{10}H_{18}O$	77.86	11.76
	0.1353	0.3863	0.1442	77.98	11.92	$C_{10}H_{18}O$	77.86	11.76

was neutralized and distilled with steam. This yielded 1.5 g of o-cymene, with a b.p. of 175-176°; d_4^{20}0.8770, n_D^{20} 1.4985. The figures given in the literature [20]: B.p. 175°, d_4^{20}0.876, n_D^{20} 1.5000.

In most instances the tertiary alcohols were dehydrated by heating the alcohol to 200° for 6 hours in sealed tubes with a 50% excess of acetic anhydride. The yield of hydrocarbons was 85-90%. The chlorine-substituted alcohol was dehydrated by distillation over P_2O_5 in vacuo. The chloride yield was 70%. Dimethyl-(1-methylcyclohexen-3-yl)-carbinol was dehydrated by distilling it with a 5% solution of oxalic acid. The hydrocarbon yield was 80%. The constants of the dehydration products are given in Table 7. The analytical findings for the substances synthesized for the first time are given below (Table 11).

Dehydration product of dimethyl-(4-chlorocyclohexen-3-yl)-carbinol: 0.1592 g substance: 0.1435 g AgCl. Found %: Cl 22.30. $C_9H_{15}Cl$. Calculated %: Cl 22.63.

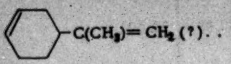
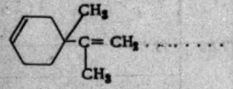
Dehydrogenation of the third substance in Table 7 in a single pass over palladinized asbestos at 300° yielded a condensate that did not decolorize bromine water, with a b.p. of 176-177°; d_4^{20} 0.8530, n_D^{20} 1.4882. The following constants are given in the literature for p-cymene [20] b.p. 177°, d_4^{20} 0.8570, n_D^{20} 1.4904.

When the dehydration product of dimethyl-(4-chlorocyclohexen-3-yl)-carbinol was passed over the catalyst under the same conditions, the hydrohalide was split out and 65% of cumene was produced. B.p. 151-153°, d_4^{20} 0.8613, n_D^{20} 1.4918. Figures in the literature [21]: B.p. 152.5°, d_4^{20} 1.8640, n_D^{15} 1.4947.

SUMMARY

1. Various findings relating to the condensation of dienes with acrolein and methyl vinyl ketone have been defined more accurately; in particular, the structure of the condensation products of isoprene with acrolein and methyl vinyl ketone and of piperylene with the last-named substance has been established.

TABLE 11

Substance		CO_2	H_2O	Found %		Formula	Calculated %	
	g	g	g	C	H		C	H
 $-C(CH_3)=CH_2$ (?) . .	0.1063	0.3460	0.1103	88.82	11.61	C_9H_{14}	88.45	11.55
	0.1183	0.3836	0.1256	88.49	11.88	$C_{10}H_{16}$	88.16	11.84

2. The action of methylmagnesium iodide and ethylmagnesium iodide upon hydroaromatic aldehydes and ketones — products of the condensation of dienes with acrolein and methyl vinyl ketone — has yielded several secondary and tertiary hydroaromatic alcohols not described previously in the literature: the isomers, homologs, and analogs of α-terpineol.

3. Dimethyl-(1-methylcyclohexen-3-yl)-carbinol, not described previously in the literature, has been synthesized by the action of methylmagnesium iodide upon the condensation product of divinyl and methyl methacrylate.

4. Several acetates of the secondary alcohols have been synthesized by acetylating these alcohols with acetic anhydride.

5. The respective hydroaromatic ketones, particularly the hitherto undescribed propionylcyclohexene-3, have been synthesized by oxidizing the secondary alcohols with a chromic acid mixture.

6. Several hydroaromatic hydrocarbons, especially 1-methyl-1-isopropenylcyclohexene-3, not previously described in the literature, have been synthesized by dehydrating the tertiary alcohols. The dehydrogenation of some of the synthesized hydrocarbons over palladium has been explored.

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[19] A.A.Petrov and N.P.Sopov. J. Gen. Chem., 18, 1781 (1948).
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Received July 15, 1950

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THE CONFIGURATION OF THE CRYSTALLINE BROMIDES OF BUTADIENE

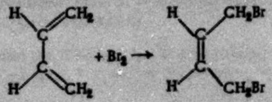
Ya.M.Slobodin and S.A.Zaboev

As we know, butadiene reacts with bromine to form two tetrabromides, with m.p. of 39 and 118°, and two dibromides, one of which is a liquid and the other is crystalline, with a m.p. of 53°. In the past, the liquid dibromide was assigned the structure of cis-1,4-dibromobutene-2, with the crystalline dibromide, m.p. 53°, assigned the configuration of trans-1,4-dibromobutene-2 [1]. It was later demonstrated that the liquid dibromide is a product of the addition of bromine to butadiene at the 3 and 4 positions. Hence, it is 3,4-dibromobutene-1 [2].

A study has been made of the transformation of the crystalline dibromide into erythrites and tetrabromobutanes in order to determine its configuration. Examination of the literature on the subject indicates that various groups are added at the double bond of the dibromide partly in the cis position and partly in the trans position [3]. Hence, these findings do not provide an unequivocal answer concerning the configuration of the dibromide.

In the present research we have investigated the Raman spectra of the butadiene bromides. Two frequencies for the C—Br bond, 593 and 628 cm^{-1}, and a frequency for the double bond, 1655 cm^{-1}, have been found in the spectrum of the crystalline dibromide with a m.p. of 53°. The 593 and 628 cm^{-1} frequencies refer to the $-CH_2Br$ group. The double-bond frequency value provides an unequivocal answer to the problem of the configuration of the crystalline dibromide, which can only be a cis form. The frequency of the C=C bond would have to be 1670 to 1680 cm^{-1} for the trans form.

These findings indicate that butadiene enters into reaction with bromine in its "bent" form, resulting in the formation of the cis-dibromide.



Turning to the problem of the configuration of the butadiene tetrabromides, we must point out that the two known crystalline forms represent the possible geometrical isomers. One of them is a meso form, while the other is a dl form.

Investigation of the Raman spectra of the tetrabromides showed that the tetrabromide with a m.p. of 39° contains four C—Br bond frequencies, 568, 608, 638, and 673 cm^{-1}, while only two frequencies were found for the C—Br bond, 568 and 598 cm^{-1}, in the spectrum of the tetrabromide with a m.p. of 118°. The 50% drop in the number of C—Br bond frequencies in the high-melting tetrabromide may be due to the presence of an axis of symmetry in its molecule. This is conceivable for the dl form, but cannot occur with the meso form.

It follows from the foregoing that the high-melting tetrabromide of butadiene has a dl configuration. The low-melting tetrabromide is the meso form.

The spectra of all the crystalline bromides were photographed in their carbon tetrachloride and acetone solutions. The solutions used were of approximately equal concentration.

SUMMARY

1. The butadiene dibromide with a m.p. of 53° is cis-1,4-dibromobutene-2.

2. The butadiene tetrabromide with a m.p. of 39° is the meso form of 1,2,3,4-tetrabromobutane.

3. The butadiene tetrabromide with a m.p. of 118° is the dl form of 1,2,3,4-tetrabromobutane.

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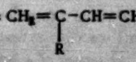
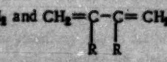
Received July 21, 1950

THE BROMINATION AND IODOXATION OF 1,1-DIALKYLBUTADIENES-1,3. VIII.

V.I.Esafov

It has been shown in our previous report [1] that dienes of the  $CH_2=C(R)-CH=CH_2$ and  $CH_2=C(R)-C(R)=CH_2$ types are examples of departures from the M.D.Lvov-D.V.Tishchenko rule, no matter whether they have one or two quaternary carbon atoms at the double bonds. Owing to the appreciable conjugation of the double bonds they add bromine principally at the 1,4-position during gentle bromination. We found it necessary to trace the course of the bromination and iodoxation reactions of dienes of the 1,1-dialkylbutadiene-1,3 type, the molecules of which are, according to the electronic theory, more polar than divinyl, which ought to promote the reaction at the 1,4 position. Study of the bromination and iodoxation of 1,1-dimethylbutadiene-1,3 and 1-methyl-1-ethylbutadiene-1,3 has shown, however, that, in contrast to the symmetrically disubstituted butadienes, viz.: hexadiene-2,4 [2] and diisopropenyl, the first of these compounds is brominated more completely and with the evolution of considerable HBr, provided all other conditions remain the same.

These new findings support the rule derived empirically [1]: that the less symmetrical the position of conjugated double bonds in a system, the greater the effect of radicals upon the degree of conjugation of these bonds. On the other hand, we observed that the 1,1-dialkylbutadienes-1,3 react readily with maleic anhydride. Thus, 1,1-dialkylbutadienes-1,3 exhibit perceptible autonomy of their double bonds during bromination and iodoxation, whereas they react like conjugated systems with maleic anhydride. It seems to us that these facts are weighty arguments against any stereotyped application of present-day hypotheses founded upon the electronic theory in explaining the reactions of organic compounds.

In support of this assertion we may cite the findings of D.V.Tishchenko [3], who found that the chlorination of aliphatic halogenated derivatives proceeds contrary to the concept of the so-called alternating effect adopted by some chemists [4].

Dienes of the 1,1-dialkylbutadiene-1,3 type were first produced in A.M.Zaitsev's laboratory [5] by dehydrating dialkylallylcarbinols with dilute sulfuric acid or by splitting out molecules of hydrogen chloride from the chlorohydrins of the carbinols. Reformatsky [6], however, assigned them the structure of dienes with independent double bonds on the basis of his study of their oxidation products with a chromic acid mixture. Slobodin [7], on the contrary, has shown that the dehydration of dialkylallylcarbinols* with dilute sulfuric acid proceeds in two directions, dienes with conjugated double bonds being principally formed, whereas diisopropylallylcarbinol is chiefly dehydrated to 2-methyl-3-isopropylhexadiene-2,5. Petrov and his students [8] have shown that dehydrating methylhexylallylcarbinol over Al_2O_3 at 290-300° results in 72% of the theoretical yield of 4-methyldecadiene-1,4, the isomeric 4-methyldecadiene-1,3 being present as an impurity. Not so long ago Favorskaya and Fridman [9] discovered the interesting fact that methylphenyl- and diphenylallylcarbinols undergo ketonic cleavage when heated with 25% H_2SO_4. Under these same conditions dimethylallylcarbinol yielded no acetone at all, on the other hand, while methylethylallylcarbinol [10] mainly underwent isomerization to a primary alcohol with the structure of $(CH_3)_2C=CH-CH_2CH_2OH$. while being dehydrated to dienes.

In view of the fact that the catalytic dehydration of dialkylallylcarbinols results in dienes with independent double bonds, while the action of sulfuric acid produces a low yield of hydrocarbons, as Slobodin has indicated, we utilized the dehydration of tertiary α,β-unsaturated carbinols with iodine to secure 1,1-dialkylbutadienes-1,3. We found that the reaction rate depends upon the amount of iodine used in the reaction, the carbinol reacting with it and liberating heat. In view of the fact that dimethylallylcarbinol, for example, is fairly stable thermally, while its decomposition sets in at the boiling point when iodine is present, it must be assumed that it is not the carbinol proper that decomposes but rather its oxonium compounds with the iodine.

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* With a greater or equal degree of hydrogenation of the carbon atoms in the alkyl groups adjacent to the carbinol group, as compared with the allyl radical.

When a compound of this sort is heated it not only turns 1,1-dimethylallylcarbinol (and to a lesser degree methylallylcarbinol) into dienes, but is also decomposed at the point where the allyl radical is connected to the carbinol carbon atom.[*] Thus, we can say that under suitable conditions and when acted upon by certain chemical agents, tertiary carbinols containing an allyl radical can be cleaved at the least stable of their C—C bonds: $RRC(OH)-\vdots-CH_2CH=CH_2$, this being a general property of theirs.

EXPERIMENTAL

1. Syntheses of dialkylallylcarbinols.[**] In accordance with Yavorsky's prescription [11], the magnesium used for these reactions was first pickled for 4 hours in allyl bromide. We used 0.5 moles of the ketones and the allyl bromide and 150 ml of absolute ether in synthesizing the carbinols. The reactions were carried out in our apparatus [1], with the stirrer in continuous operation. The reaction flask was chilled with snow at the very outset of the synthesis until the violent reaction ceased. The ketones and the allyl bromide were added separately by dropping during the course of 4 hours, after which the mass was stirred for another 1 hour. After the mass had been allowed to stand at rest for an hour, the reaction product was decomposed with ice and then with aqueous ammonia. The yield of dimethylallylcarbinol averaged 43.2% of the theoretical; its b.p. was 117-118° (732 mm); d_4^{20} 0.8308; n_D^{20} 1.4300; MR_D 31 12, calculated 31 08.

The yield of methylethylallylcarbinol was 42.9% of the theoretical, its b.p. being 138-139° (735 mm); d_4^{20} 0.8323; n_D^{20} 1.4310; MR_D 35.73; calculated 35.70.

The iodine numbers of the carbinols were determined by the MacIlhinney method, which yielded fairly dependable results (Table 1).

2. Experiments on the dehydration of dialkylallylcarbinols. a) No dehydration occurred when the vapor of 10 g of dimethylallylcarbinol was passed through a glass coil heated to 290° for 20 minutes.

b) Dehydrating dimethylallylcarbinol with sulfanilic acid yielded only little of the dienes. In view of the fact that dehydrating dialkylallylcarbinol with either sulfanilic acid or dilute sulfuric acid [7] produced low yields of dienes, we proceeded to test dehydrating the carbinols in the presence of iodine.

c) When dimethylallylcarbinol was distilled rapidly with a crystal of iodine, the dehydration was negligible.

d) Subsequent dehydration experiments were performed in the following apparatus, designed to increase the time during which the carbinol was in contact with the iodine. A round-bottomed flask was connected to a water trap of a Dean-Stark apparatus. A 70-cm herringbone dephlegmator, terminated with a thermometer, was placed in the trap. The dephlegmator was connected to a condenser, the end of which was connected via an adapter with a gas outlet tube to the collector and to a gasometer.

When 26 g of dimethylallylcarbinol was boiled with 0.02 g of iodine, the first thing noticed was the evolution of gas, 46.3 ml of it (at 20° and 740 mm) being collected, after which the liquid began to distil slowly, the reading of the thermometer in the dephlegmator not rising above 80°. The distillation of the liquid felt off after 1.5 hours of heating. After 2 hours of heating, another 0.2 g of iodine was placed in the flask, 50 ml more of gas being evolved and the liquid distilling rapidly, distillation coming to an end after 1 hour had elapsed. These tests show that the extent of dehydration of this carbinol depends upon the quantity of iodine used as well as upon the increase of the time of contact with the iodine.

The gas was found to contain 2.2% by volume of propylene. The liquid distillate was treated with 15 ml of water to eliminate the water-soluble substances. The first distillation of the hydrocarbon layer yielded the following fractions: 1) 56-65° — 2.9 g; 2) 65-75° — 7.5 g; and 3) 75-76° — 3.5 g.

The wash-water liquid was mixed with the aqueous liquid in the trap (see below). The residue left in the flask and the 4 g of liquid organic product collected in the trap were treated with a potassium iodide solution to remove the iodine, washed with water, and dried with anhydrous sodium sulfate (see below).

e) The experiment was repeated, adding 1 g of sublimed anhydrous iodine to 26 g of the dimethylallylcarbinol; intensive local heating, with crepitation, being observed. When the mixture was boiled, 140 ml

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[*] We observed this fact in 1948 in association with O.G.Boyarshinova.

[**] In association with O.G.Boyarshinova and L.P.Lebedeva.

TABLE 1

Bromination of Dialkylallylcarbinols and of Their Dehydration Products

Test No.	Wt. g	Ml of Br$-$CCl$_4$ solution	Ml of 0.1 N H_2SO_4 solution			Overall iodine number	Iodine number of splitting	Iodine number proper	Halogen converted into HBr as % of total halogen consumption
			Used to titrate excess halogen	Equiv.consumption of I for sample	Used to titrate I in HI				
	Dimethylallylcarbinol						By theory	253.61	
1	0.0852	9.0	48.58	17.52	0.47	261.01	14.0	247.01	
2	0.0766	9.0	50.84	15.26	0.41	252.86	13.58	239.28	
	Methylethylallylcarbinol						By theory	222.28	
1	0.0642	6.1	27.40	11.40	0.39	225.39	15.42	209.97	
2	0.0672	6.1	26.62	12.80	0.39	230.06	14.58	215.48	
	Hydrocarbon with b.p. of 56-59°						By theory	618.56	
1	0.1185	7.3	0.14	30.14	1.27	322.84	27.20	295.64	4.21
2	0.1116	13.0	13.14	40.78	2.06	463.81	46.85	416.96	5.05
	1,1-Dimethylbutadiene-1,3						By theory	618.56	
1	0.1608	9.4	0.02	36.86	2.59	290.96	40.88	250.08	7.02
2	0.1023	12.1	11.38	36.10	4.22	447.91	104.72	343.19	11.66
	Hydrocarbon with b.p. of 90-92°						By theory	528.34	
1	0.0894	4.5	0.08	18.48	0.83	262.37	23.56	238.81	4.49
2	0.0614	6.2	8.90	16.68	0.63	344.82	26.04	318.78	3.77
	Hydrocarbon with b.p. of 108-110°						By theory	528.34	
1	0.0926	4.8	0.04	19.68	0.48	269.76	13.15	256.61	2.43
2	0.0768	8.0	15.12	17.76	0.80	293.52	26.44	267.08	4.50

of gas (at 20° and 740 mm) was first given off, and then the liquid distilled rapidly. The dehydration process was completed within 15 minutes. The subsequent operations were the same as in Experiment d. The residue in the reaction flask and the trap totaled 7.5 g. The first fractionation of the liquid distillate yielded the following fractions: 1) 56-65° – 1.6 g; 2) 65-75° – 5.2 g; 3) 75-100° – 1.7 g; and above 100° – 2.7 g.

Comparison of the results of experiments d and e indicates that increasing the amount of iodine placed in the reaction accelerates the dehydration of the carbinol, but also increases the quantity of by-products.

The aqueous wash liquids of the two experiments were combined, salted out with sodium chloride, and reduced to two-thirds of their volume by distillation. The distillate was a two-layer liquid, the lower, aqueous layer exhibiting an iodoform reaction, proving that acetone was present as the result of the decomposition of the dimethylallylcarbinol into acetone and propylene. This was likewise proved by the formation of acetone condensation products, contained in the carbinol decomposition residues. Fractionation of the residues of the two experiments yielded the following fractions: 1) up to 122° – 1.5 g; 2) 122-135° – 1.3 g; 3) 135-225° – 2 g; and 4) 5 g of a dark residue. The 122-135° and 135-225° fractions were each boiled for two hours with 6 ml of a 0.2 N solution of NaOH.

After this heating of the reaction products, the aqueous solutions were driven off, the distillates being filtered through moist filters and diluted to 10 ml with water, after which they were tested for acetone, the presence of which was demonstrated by an iodoform reaction as well as by a V. V. Chelintsev – Nikitin reaction [12].

Thus, the discovery of a negligible amount of gas, and particularly the finding of acetone and of its condensation products, proved that the dimethylallylcarbinol was cleaved at the C – C bond between the allyl radical and the carbinol carbon atom.

Further repeated fractionation of the combined hydrocarbon fractions at 745 mm yielded the following fractions: 1) 56-59° – 3.0 g; 2) 59-75° – 5.7 g; and 3) 75-76° – 6.8 g.

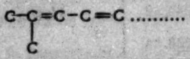
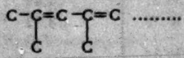
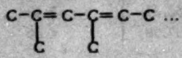
The hydrocarbon with a b.p. of 56-59° had d_4^{20} 0.7001; n_D^{20} 1.4029; MR_D 28.60. The hydrocarbon with a b.p. of 75-76° had d_4^{20} 0.7196; n_D^{20} 1.4432; MR_D 30.25. $C_6H_{10}\Gamma_2$. Calculated 28.974; the exaltation was +1.276.

Bromination of the hydrocarbon with a b.p. of 56-59° (see Table 1) (without using an excess of the bromine solution) indicated that the molecule had more than one double bond. Oxidizing the hydrocarbon with permanganate at 0° yielded acetone and formic acid. After the volatile acids had been driven off, we were unable to find any dibasic acids in the residue. These findings proved that the hydrocarbon with a b.p. of 56-59° contained 2-methylpentadiene-1,4 with a possible trace of diallyl.

Bromination of the hydrocarbon with a b.p. of 75-76° (Table 1) indicated that its double bonds had less autonomy than in its more highly substituted analog (Table 2), though its autonomy was high enough, compared to the symmetrically disubstituted butadienes-1,3.

TABLE 2

Comparison of the Bromination Data for Some Dienes

No.	Molecular carbon skeletons	At a quantity of Br — CCl_4 solution sufficient to saturate the double bonds completely	
		Overall iodine numbers, % of theoretical	Halogen converted into HBr, as % of total halogen consumption
1	 $C-\underset{\overset{|}{C}}{C}=C-C=C$	72.2	11.6
2	 $C-\underset{\overset{|}{C}}{C}=C-\underset{\overset{|}{C}}{C}=C$	76.2	17.0
3	 $C-\underset{\overset{|}{C}}{C}=C-\underset{\overset{|}{C}}{C}=C-C$ ...	81.7	24.1

The presence of conjugated double bonds in this hydrocarbon can be readily proved by its reaction with maleic anhydride dissolved in toluene. The reaction produces a yellow color, accompanied by the evolution of considerable heat. The ampoule was heated for 2 hours on a boiling water bath to complete the reaction. After the reaction product had been treated with alkali and the toluene had been driven off, the potassium salts were decomposed with dilute sulfuric acid. As the solution was chilled, 1,1-dimethylcyclohexen-2-dicarboxylic acid-5,6 crystallized out. Our findings agree with those of Slobodin [7], but contradict those of Gorin and his associates [13], who, referring to Farmer and Worren [14], state that 2-methylpentadiene-2,4 yields a yellowish amorphous mass (polymer product) when treated with maleic anhydride.

When the hydrocarbon with a b.p. of 75-76° was oxidized with permanganate at 0°, the neutral products contained acetone, and the volatile acids contained formic acid, 1.5 g of the hydrocarbon yielding 0.46 g of the acid. These findings indicate that the hydrocarbon with a b.p. of 75-76° is 1,1-dimethylbutadiene-1,3.

3 Experiments on dehydrating methylethylallylcarbinol in the presence of iodine. This hydrocarbon was dehydrated as we dehydrated the hydrocarbon of Experiment 2, using 0.2 g of anhydrous, sublimed iodine for 28.5 g of the carbinol. The whole process was completed within 25 minutes. The liquid distillate totaled 20.6 g, and the residue in the flask and the trap totaled 3.5 g. The aqueous liquid left after the distillate had been treated with water did not exhibit an iodoform reaction (after 20 minutes of standing). After the hydrocarbon layer had been dried with $CaCl_2$, it was repeatedly distilled (727 mm) over Na in a current of anhydrous CO_2. This yielded the following fractions: 1) up to 90° — 1 g; 2) 90-92° — 4.0 g; 3) 92-95° — 1.6 g; 4) 95-108° — 2.1 g; 5) 108-110° — 3.2 g; and a residue of 0.6 g. The hydrocarbon with a b.p. of 90-92° had d_4^{20} 0.7324; n_D^{20} 1.4180; MR_D 33.06. The hydrocarbon with b.p. 108-110° had d_4^{20} 0.7558; n_D^{20} 1.4523; MR_D 34.32. $C_7H_{12}\Gamma_2$ calculated 33.59. The exaltation was 0.73. These hydrocarbons were brominated (Table 1), the hydrocarbon with a b.p. of 90-92° exhibiting more than one double bond in its molecule. On the other hand, the hydrocarbon with a b.p. of 108-110° was brominated like a diene, with appreciable conjugation of double bonds, differing sharply from 1,1-dimethylbutadiene-1,3. Iodoxation of the hydrocarbon with a b.p. of 108-110° is, however, fully like that of 1,1-dimethylbutadiene (Table 3) and is accompanied by even greater conversion of iodine into HI, as is typical of dienes with slight conjugation of double bonds.

Such differing behavior of the hydrocarbon with a b.p. of 108-110° in the bromination and iodoxation reactions deserved special investigation. In contrast to the hydrocarbon with a b.p. of 90-92°, that with a b.p. of 108-110° reacted with a solution of maleic anhydride in toluene, evolving considerable heat. We secured a high

TABLE 3

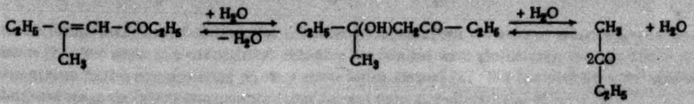
Iodoxation of Dienes

Test No.	Weight, grams	Ml of 0.1 N $Na_2S_2O_3$ solution			Iodine number	Per cent iodine converted into HI
		Used to titrate excess iodine	Equivalent consumption of I for the sample	Used to titrate iodine in HI		
	1,1-Dimethylbutadiene-1,3					
1	0.0812	9.96	18.90	9.60	295.44	50.78
2	0.1275	84.79	49.56	33.70	493.38	67.99
	Hydrocarbon with a b.p. of 108-110°					
1	0.0798	13.82	15.04	12.43	239.22	82.64
2	0.1438	84.70	49.55	41.32	438.25	83.22

yield of the supposed 1-methyl-1-ethylcyclohexene-2-dicarboxylic acid-5,6, with m.p. of 170°. Its Ag salt was produced by saturating the acid with silver carbonate and then evaporating the solution on a boiling water bath. Analysis of the Ag salt,* dried at 85°, yielded the following figures:

0.1743 g substance: 0.0836 g Ag. Found %: Ag 47.96. $C_{11}H_{14}O_4Ag_2$. Calculated %: Ag 50.66.

Study of its properties as well as the analogy of its behavior to that of the dimethyl- and methylethylallylcarbinols indicated that the hydrocarbon with a b.p. of 108-110° consisted chiefly of 1-methyl-1-ethylbutadiene-1,3. The dark residue left in the flask after the iodine had been removed and the remainder dried was fractionated. The fraction with a b.p. of 155-170° displayed a positive iodoform reaction, indicating that it contained the condensation products of methyl ethyl ketone in the most likely form of 3-methylhepten-3-one-5. Though this latter ketone was an ethyl ketone, as an α,β-unsaturated ketone it was hydrolytically cleaved in the presence of a 1 N NaOH solution, yielding methyl ethyl ketone, which was the basis for the positive iodoform reaction:



$$C_2H_5-\underset{\displaystyle CH_3}{\underset{|}{C}}=CH-COC_2H_5 \underset{-H_2O}{\overset{+H_2O}{\rightleftarrows}} C_2H_5-\underset{\displaystyle CH_3}{\underset{|}{C}}(OH)CH_2CO-C_2H_5 \overset{+H_2O}{\rightleftarrows} 2\,\begin{matrix}CH_3\\|\\CO\\|\\C_2H_5\end{matrix} + H_2O$$

SUMMARY

1. It has been shown that dialkylallylcarbinols are dehydrated in the presence of iodine in two ways, yielding dienes with independent as well as conjugated double bonds. A decrease in the degree of hydrogenation of the alkyl groups attached to the carbinol carbon atoms lowers the yield of the latter dienes.

2. It has been shown that, in contrast to diisopropenyl and hexadiene-2,4, the double bonds are less conjugated in 1,1-dimethylbutadiene-1,3, so that its bromination and iodoxation reactions are more complete.

3. It has been shown that the ability of tertiary alcohols containing an allyl radical to be cleaved at the bond between the allyl radical and the carbinol carbon atom is a general property of these alcohols.

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*) Contained the acid Ag salt as an impurity.

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Received July 8, 1950

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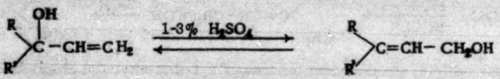
DERIVATIVES OF ACETYLENE

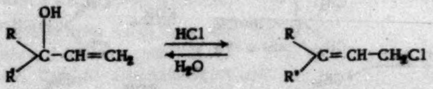
135. REARRANGEMENT OF AN ALLYLIC SYSTEM. V. EXCHANGE REACTIONS OF γ,γ-DIMETHYLALLYL CHLORIDE WITH AMINES, POTASSIUM CYANIDES, AND SALTS OF ORGANIC ACIDS

I. N. Nazarov, V. N. Rakcheev, and L. I. Shmonina

We have shown earlier that compounds that contain a dialkylallyl radical are distinguished by extremely high mobility and tendency to allyl rearrangments. The α,α- and γ,γ-dialkylallylcarbinols are reversibly isomerizable into one another by dilute solutions of sulfuric acid even at room temperature, [1]:

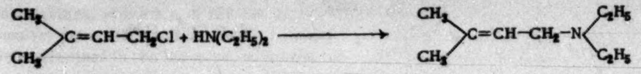


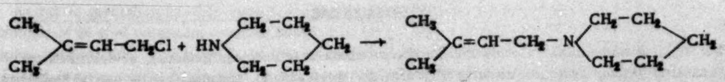
The rearrangement of the dialkylallyl group takes place most readily in some exchange reactions. When dialkylvinyl carbinols are reacted with hydrogen chloride, for example, the principal reaction products are primary α,α-dialkylallyl chlorides, while hydrolysis of the latter causes reversible rearrangement, the dialkylvinylcarbinols being formed again [2]:



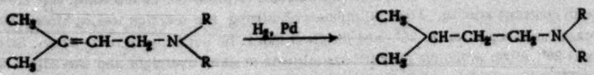
The exchange reactions of dialkylallyl chlorides with potassium acetate are likewise accompanied by rearrangements [2]. But when γ,γ-dialkylallyl chlorides are reacted with alcoholates, the reaction is normal, without any rearrangement, the corresponding primary esters being formed [2]. Nor is rearrangement observed to occur when Grignard reagents (phenylmagnesium bromide) act upon γ,γ-dimethylallyl bromide [3].

In the light of these facts, it was found desirable to investigate the exchange reactions of γ,γ-dialkylallyl chlorides with amines, salts of organic acids, and potassium cyanide to determine the influence of the nature of the reagents upon the allyl rearrangements. We found that when γ,γ-dimethylallyl chloride is reacted with diethylamine and piperidine, the exchange reaction is normal, without any isomerization, a high yield of the respective tertiary amines, containing the γ,γ-dimethylallyl radical being produced:

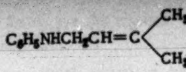




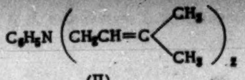
We were unable to find any isomeric tertiary amines, containing a α,α-dimethylallyl radical, in the reaction products. The structure of the synthesized amines was established by hydrogenating them over a Pd catalyst, one molecule of hydrogen being absorbed, which converted them into the known isoamylamines:



γ,γ-Dimethylallyl chloride behaves similarly when reacted with aniline. A mixture of secondary and tertiary amines (I and II) is produced, which is extremely hard to separate:

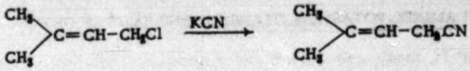


(I)



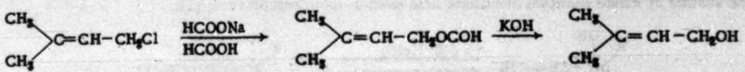
(II)

Reacting γ,γ-dimethylallyl chloride with a saturated aqueous solution of potassium cyanide, we again secured a low yield of nothing but the normal reaction product – γ,γ-dimethylallyl cyanide:

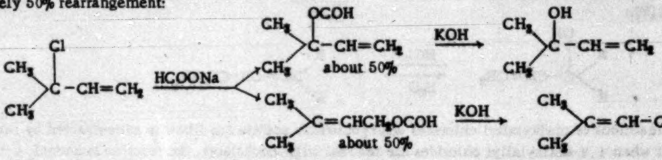


This reaction is largely obscured, however, by side processes, chiefly hydrolysis of the chloride.

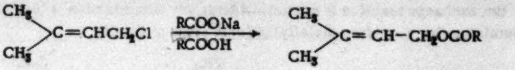
It is worthy of note that the reaction involves no rearrangement when the γ,γ-dimethylallyl chloride is reacted with sodium formate, either, a high yield of the formate of a primary γ,γ-dimethylallyl alcohol being produced, saponification of which with an aqueous alkali yields the γ,γ-dimethylallyl alcohol itself:



As we have shown previously[2], the analogous reaction of γ,γ-dimethylallyl chloride with potassium acetate is accompanied by approximately 30% rearrangement. The reaction of sodium formate with the tertiary α,α-dimethylallyl chloride, however, yields a mixture of nearly equal proportions of the tertiary and primary formates, so that here, as in the reaction with potassium acetate [2], the process involves an approximately 50% rearrangement:



It is much harder to carry out an exchange reaction of γ,γ-dimethylallyl chloride with salts of the higher organic acids than with acetates, or, especially, formates; the only one we have been able to isolate in the pure state is the propionate of γ,γ-dimethyl allyl alcohol. Nor are these reactions accompanied by practically any rearrangements, the principal products being esters of the primary γ,γ-dimethylallyl alcohol:



R = C_2H_5; C_3H_7

EXPERIMENTAL

The γ,γ-dimethylallyl chloride used for the exchange reactions was produced, as described previously [2], by reacting gaseous hydrogen chloride with dimethylvinylcarbinol, prepared by the partial hydrogenation of dimethylacetenylcarbinol [4].

Reaction of γ,γ-dimethylallyl chloride with diethylamine. 59 g of freshly distilled diethylamine (b.p. 56-57°) was placed in a three-necked, round-bottomed flask, fitted with a thermometer, a dropping funnel, and a mechanical stirrer, and 42 g of γ,γ-dimethylallyl chloride (b.p. 58-60° at 150 mm; n_D^{20} 1.4475) was added drop by drop with constant stirring. After 40 minutes of stirring, the reaction was so violent that the temperature of the reaction mixture rose to 75°, and the flask had to be cooled with cold water. Stirring was continued for 6 hours at 20°, after which the product was allowed to stand overnight and was stirred the next day for 3 hours at 70-75°. The precipitated diethylamine hydrochloride (20 g) was filtered out and washed with ether, the product being fractionated at a low vacuum at first, and then at atmospheric pressure. This yielded 35 g of diethyl-γ,γ-dimethylallylamine as a colorless liquid with the strong specific odor of a base and a b.p. of 158-160°.

n_D^{20} 1.4390; d_4^{20} 0.7911; MR_D found 47.0; calculated 47.2.

5.749 mg substance: 0.482 ml N_2 (25°, 745 mm). 3.855 mg substance: 0.325 ml N_2 (25°, 745 mm).
Found %: N 9.41, 9.47. $C_9H_{19}N$. Calculated %: N 9.90.

The picrate of this amine was readily formed by reacting it with an alcoholic solution of picric acid; it had a m.p. of 101-102° after recrystallization from alcohol. When 10 g of the amine, dissolved in methanol, was hydrogenated with a Pd catalyst, 1800 ml of hydrogen (18°, 746 mm) was absorbed instead of the 1760 ml called for theoretically. Fractionation of the hydrogenation product yielded 7 g of the dimethylisoamylamine described in the literature [5], with a b.p. of 152-153°; n_D^{20} 1.4180. The m.p. of the picrate of this amine was 74-75° (from alcohol), in agreement with the figure given in the literature [5].

Reaction of γ, γ-dimethylallyl chloride with piperidine. We took 25 g of freshly distilled piperidine (b.p. 102-104°) and added 15 g of γ, γ-dimethylallyl chloride a drop at a time. The mixture was stirred for 8 hours at room temperature, set aside to stand overnight, and then again stirred for 8 hours at 65-70° the next day. The precipitated piperidine hydrochloride was filtered out and washed with ether, the product being fractionated, in vacuo at first and then at standard pressure. This yielded 15.3 g of γ, γ-dimethylallylpiperidine, with a b.p. of 79-80° at 14 mm and 193-194° at atmospheric pressure.

n_D^{20} 1.4700; d_4^{20} 0.8586; MR_D found 49.82; calculated 49.65.

5.820 mg substance: 0.469 ml N_2 (23°, 745 mm). 6.610 mg substance: 0.542 ml N_2 (22°, 737 mm).
Found %: N 9.11, 9.20. $C_{10}H_{19}N$. Calculated %: N 9.15.

The picrate of γ, γ-dimethylallylpiperidine fused at 145-146° (from alcohol). When 6 g of γ, γ-dimethylallylpiperidine was hydrogenated in an ethyl alcohol solution over a Pd catalyst, 980 ml of hydrogen (21°, 753 mm) was absorbed, instead of the 978 ml called for theoretically. Fractionation yielded 5 g of isoamylpiperidine, with a b.p. of 72-73° at 14 mm.

n_D^{20} 1.4460; d_4^{20} 0.8249; MR_D found 50.28; calculated 50.02.

6.105 mg substance: 0.491 ml N_2 (22°, 740 mm). 6.125 mg substance: 0.496 ml N_2 (22°, 744 mm).
Found %: N 9.06, 9.17. $C_{10}H_{21}N$. Calculated %: N 9.03.

The picrate of isoamylpiperidine fuses at 136-137° (from alcohol) and exhibits no depression of the mixed melting point with a synthetic sample.

Reaction of γ, γ-dimethylallyl chloride with aniline. We took 27 g of freshly distilled aniline (b.p. 179.5°) and added 15 g of the chloride, dissolved in 30 ml of anhydrous ether, a drop at a time. The mixture was stirred for 6 hours at room temperature, let stand overnight, and then stirred again for 3 hours at 50° and for 6 hours at 60-65°. The aniline hydrochloride was filtered out, the precipitate washed with ether, and the product fractionated in vacuo. This yielded the following fractions (at 14 mm): I-b.p. 130-135°, 8 g; n_D^{20} 1.5548; II-b.p. 135-170°, 4 g; n_D^{20} 1.5463.

Fraction I consisted chiefly of γ, γ-dimethylallylaniline (I), hydrogenation of which yielded the known isoamylaniline, with a b.p. of 126-130° at 16 mm and n_D^{20} 1.5305 [6]. Fraction II was a mixture of the secondary and tertiary amines (I and II). When it was hydrogenated, it yielded 1.5 g of the diisoamylaniline described in the literature, with a b.p. of 147-150° at 16 mm and n_D^{20} 1.5230 [7].

Action of potassium cyanide upon γ, γ-dimethylallyl chloride. 20 grams of the chloride was added to a solution of 26 g of potassium cyanide in 40 ml of water. The mixture was stirred vigorously for 5 hours at room temperature. The product was extracted with ether, dried with magnesium sulfate, and fractionated, at a low vacuum to begin with and then at atmospheric pressure. This yielded 2 g of the γ, γ-dimethylallyl cyanide described in the literature [8], a liquid with a very sharp nitrile odor, and a b.p. of 97-99° at 112 mm and 162-165° at atmospheric pressure.

n_D^{20} 1.4360; d_4^{20} 0.8572; MR_D found 29.02, calculated 29.21.
Found %: N 14.85, 14.80. C_6H_9N. Calculated %: N 14.74.

In addition to the nitrile, we secured about 2 g of dimethylvinylcarbinol in this experiment, formed as the result of the hydrolysis of the γ, γ-dimethylallyl chloride.

Reaction of sodium formate with γ, γ-dimethylallyl chloride. 41 grams of sodium formate was dissolved in 120 ml of anhydrous formic acid, and 52 g of γ, γ-dimethylallyl chloride (b.p. 56-57° at 140 mm; n_D^{20} 1.4460) was added to the chilled solution with constant stirring. The mixture was stirred for 2 hours at room temperature (25°). The liquid, which layered at first, became wholly homogeneous later, a heavy precipitate of sodium chloride settling out (29 g). The product was filtered, diluted with water, extracted with ether, washed with a bicarbonate solution, dried with sodium sulfate, and fractionated, at a low vacuum (50 mm) to begin with and then at standard pressure. This yielded 26 g of the formate of γ,γ-dimethylallyl alcohol, a colorless, mobile liquid with a sweetish odor of chloroform and a b.p. of 59-60° at 50 mm and of 131-132° at 700 mm.

n_D^{20} 1.4320; d_4^{20} 0.9329. MR_D found 31.70; calculated 31.10.
8.220 mg substance: 18.91 mg CO_2; 6.68 mg H_2O. 4.965 mg substance: 11.43 mg CO_2; 4.26 mg H_2O. Found %: C 63.0, 62.8; H 9.1, 9.2 $C_6H_{10}O_2$. Calculated %: C 63.1; H 8.8.

When the sodium formate is reacted with the γ,γ-dimethylallyl chloride while heated (55-60°), much of the product becomes tarred.

Saponifying the formate of γ,γ-dimethylallyl alcohol.

a) 6 g of the formate described above was mixed with a solution of 3.5 g of potassium hydroxide in 50 ml of water, and the mixture was stirred vigorously for 6 hours at room temperature and then for 12 hours at 50°. After the aqueous layer had been saturated with potash, the product was extracted with ether, dried with potash, and fractionated. This yielded 4 g of γ,γ-dimethylallyl alcohol, with a b.p. of 138-139° at 700 mm; n_D^{20} 1.4420.

b) 52 grams of γ,γ-dimethylallyl chloride was added to 41 g of sodium formate dissolved in 120 ml of anhydrous formic acid, and the mixture was stirred at room temperature for 2 hours. The precipitated sodium chloride (29 g) was filtered out, and the product diluted with water (300 ml), extracted with ether, washed with a bicarbonate solution, and dried with sodium sulfate. The formate of γ,γ-dimethylallyl alcohol secured after the ether had been driven off was saponified without being distilled, as described above, using a 10% solution of potassium hydroxide (300 ml). Thorough fractionation of the hydrolysis products into a column yielded 1,2 g of α,α-dimethylallyl alcohol (b.p. 90-94° at 710 mm; n_D^{20} 1.4125) and 26 g of γ,γ-dimethylallyl alcohol (b.p. 139-140° at 710 mm; n_D^{20} 1.4410).

The α,α-dimethylallyl alcohol was most likely produced in this experiment by the hydrolysis of the unreacted γ,γ-dimethylallyl chloride.

Action of sodium formate on α,α-dimethylallyl chloride. 23.5 grams of α,α-dimethylallyl chloride (b.p. 36-38° at 140 mm; n_D^{20} 1.4180), was added to a solution of 18 g of sodium formate in 60 ml of anhydrous formic acid, and the mixture was stirred for 3 hours at room temperature (20°). The product was processed like the preceding one, the resultant formate being saponified with a 10% solution of potassium hydroxide (150 ml) as described above, without distillation. Thorough fractionation of the saponification products yielded 4.5 g of dimethylvinylcarbinol (b.p. 93-96° at 710 mm; n_D^{20} 1.4130) and 5 g of γ,γ-dimethylallyl alcohol (b.p. 138-140° at 710 mm; n_D^{20} 1.4420).

Reaction of sodium propionate with γ,γ-dimethylallyl chloride. 25 grams of sodium propionate was dissolved in 75 ml of propionic acid (b.p. 138-141°), and to the solution was added 26 g of its chloride (b.p. 57-60° at 150 mm; n_D^{20} 1.4460). The homogeneous mixture was stirred for 2 hours at room temperature (20°), 12 hours at 50-60°, and 10 hours at 70-80°. The 14.4 g of precipitated sodium chloride was filtered out, and the product diluted with water, extracted with ether, washed with a bicarbonate solution, and fractionated, in vacuo at first and then at atmospheric pressure. This yielded 11 g of the propionate of γ,γ-dimethylallyl alcohol as a colorless, mobile, fragrant liquid with a b.p. of 162-164° at 710 mm.

n_D^{20} 1.4310; d_4^{20} 0.9111; MR_D found 40.35; calculated 40.34.
4.46 mg substance: 11.02 mg CO_2; 4.25 mg H_2O. 4.91 mg substance: 12.13 mg CO_2; 4.61 mg H_2O. Found %: C 67.4, 67.3; H 10.3, 10.2. $C_8H_{14}O_2$. Calculated %: C 67.6; H 9.9.

Saponifying the propionate of γ,γ-dimethylallyl alcohol. 4 grams of the propionate described above was stirred vigorously with 30 ml of 10% aqueous potassium hydroxide for 3 hours at room temperature and 16 hours at 50°. The product was extracted with ether, dried with potash, and fractionated. This yielded 2.2 g of γ,γ-dimethylallyl alcohol, with a b.p. of 137-139° at 700 mm and n_D^{20} 1.4410.

Reaction of γ,γ-dimethylallyl chloride with sodium butyrate. 60 grams of sodium butyrate was dissolved in 150 ml of butyric acid, 52 g of γ,γ-dimethylallyl chloride was added, and the mixture was stirred for 10 hours at 70-80°. The precipitated sodium chloride (24 g) was filtered out, and the solution was reheated to 70-80° for 16 hours. The precipitated 3.5 g of sodium chloride was filtered out, and the solution was reheated for another 8 hours at 70-80°, but no more sodium chloride was precipitated. The product was diluted with water (300 ml), extracted with ether, washed with a soda solution, and dried with sodium sulfate. The butyrate of γ, γ-dimethylallyl alcohol secured after the ether had been driven off was saponified with an aqueous alkali (200 ml of 10% sodium hydroxide, 6 hours of heating to 80°). Extraction of the saponification products with ether, drying, and careful fractionation yielded 6 g of dimethylvinylcarbinol (b.p. 92-95° at 700 mm; n_D^{20} 1.4120) and 20 g of γ, γ-dimethylallyl alcohol (b.p. 137-139° at 700 mm; n_D^{20} 1.4410).

SUMMARY

The reaction of γ, γ-dimethylallyl chloride with diethylamine and piperidine yields about 70% of the respective tertiary amines, containing a γ, γ-dimethylallyl radical. These exchange reactions are normal, not involving allyl rearrangements. γ, γ-dimethylallyl chloride reacts similarly with potassium cyanide, producing a yield of some 10% of γ, γ-dimethylallyl cyanide, and with sodium formate, producing about 50% of the formate of γ, γ-dimethylallyl alcohol.

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Received June 2, 1950

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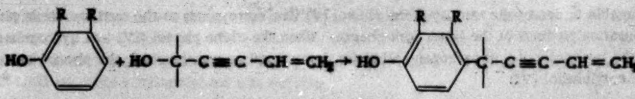
DERIVATIVES OF ACETYLENE

136. CONDENSATION OF 5-METHYL-1,3-HEXADIEN-5-OL AND 5-METHYLHEXAN-5-OL WITH PHENOL IN THE PRESENCE OF PHOSPHORIC ACID

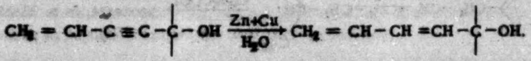
I. N. Nazarov and A. I. Kakhniashvili

In our laboratory we previously condensed phenols with vinylacetylenic alcohols, thus synthesizing for the first time substitution derivatives of phenol with a vinylacetylenic structure [1]:



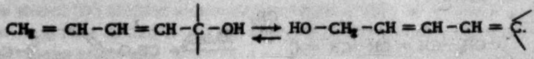
R = H or CH_3

We were also interested in investigating the condensation of phenols with 1,3-diene alcohols, which are produced by the selective hydrogenation of vinylacetylenic alcohols with coppered zinc dust and water [2]:



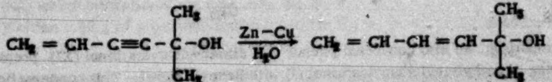
$$CH_2=CH-C\equiv C-\overset{|}{\underset{|}{C}}-OH \xrightarrow[H_2O]{Zn+Cu} CH_2=CH-CH=CH-\overset{|}{\underset{|}{C}}-OH.$$

No work at all has been done up to the present time on the condensation of 1,3-diene alcohols with aromatic compounds and with phenols in particular. These condensations are likewise of interest because the 1,3-diene alcohols readily undergo diene rearrangements when acted upon by acids, the hydroxyl group being shifted to the delta position and two double bonds being displaced, as has been demonstrated on numerous occasions in our laboratory [3]:



$$CH_2=CH-CH=CH-\overset{|}{\underset{|}{C}}-OH \rightleftarrows HO-CH_2-CH=CH-CH=C<.$$

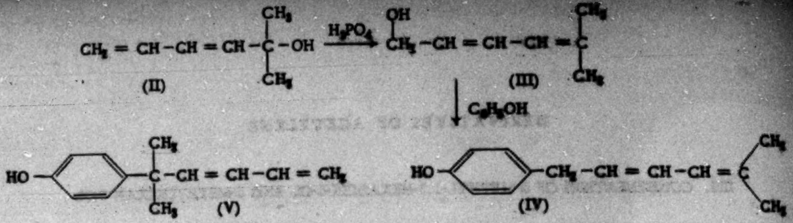
We were interested in determining how these diene rearrangements would affect the condensation of 1,3-diene alcohols with phenols when acids were present. To test these condensations we chose, first of all, the most readily available 5-methyl-1,3-hexadien-5-ol (II), prepared by the selective hydrogenation of dimethylvinylethynylcarbinol (I) [2]:



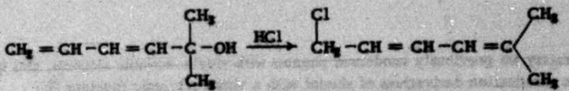
$$CH_2=CH-C\equiv C-\overset{CH_3}{\underset{CH_3}{C}}-OH \xrightarrow[H_2O]{Zn-Cu} CH_2=CH-CH=CH-\overset{CH_3}{\underset{CH_3}{C}}-OH$$

(I) (II)

When phosphoric acid is present, the diene carbinol (II) condenses with phenol much more vigorously than does the vinylacetylenic alcohol (I), resulting in the formation of a para-substituted diene phenol (IV), which corresponds to the isomeric primary diene carbinol (III) rather than to the original tertiary diene alcohol (II):

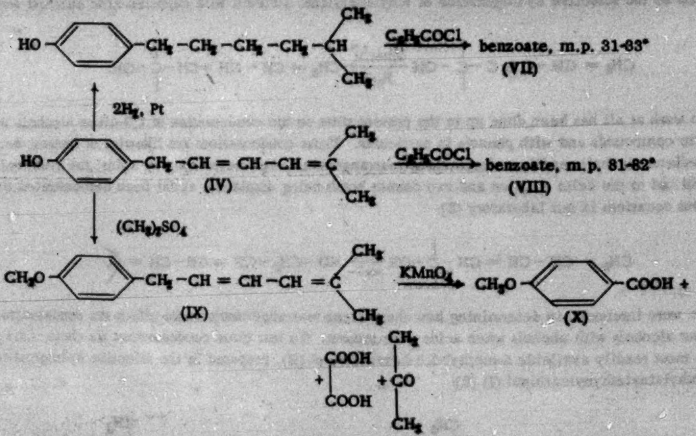


Hence, the condensation of phenol with the tertiary diene alcohol (III) involves a diene isomerization, such as occurs when this carbinol is acted upon by hydrogen chloride [4]:

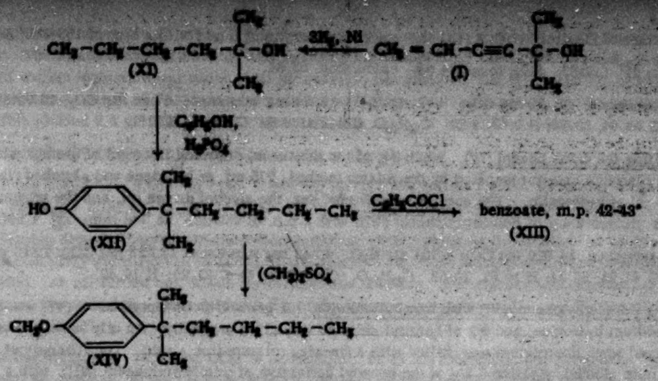


We were unable to detect the tertiary diene phenol (V) that corresponds to the tertiary diene phenol (II) in the condensation products of the latter with phenol. When the diene phenol (IV) was hydrogenated with a Pd catalyst, the two molecules of hydrogen called for theoretically were absorbed, the phenol being converted into p-isoheptylphenol (VI).

Methylation of the diene phenol (IV) with dimethyl sulfate yielded its methyl ether (IX), oxidation of which with permanganate yielded anisic acid (X), oxalic acid, and acetone. Benzoylation of the phenols (IV) and (VI) with benzoyl chloride yielded the corresponding crystalline benzoates (VII) and (VIII).



By way of comparison, we also condensed phenol with dimethylbutylcarbinol (XI), prepared by exhaustively hydrogenating dimethylvinylethynylcarbinol (I) with Raney's nickel. This condensation yielded the dimethylbutyl-p-hydroxyphenylmethane (XII), previously described in the literature [5], which was converted into the corresponding crystalline benzoate (XII) and methyl ether (XIV).



EXPERIMENTAL

5-Methyl-1,3-hexadien-5-ol was prepared by hydrogenating dimethylvinylethynylcarbinol with coppered zinc dust and water, as described previously [2]. The traces of the original dimethylvinylethynylcarbinol were eliminated from the hydrogenated product by heating the latter with 1% powdered potassium hydroxide at 110-130° until no more vinylacetylene was evolved.

Condensation of 5-methyl-1,3-hexadien-5-ol with phenol in the presence of phosphoric acid. 11 grams of 5-methyl-1,3-hexadien-5-ol (b.p. 45-47° at 12 mm; n_D^{20} 1.4720) was added drop by drop, with constant stirring, at room temperature to a mixture of 9 g of phenol and 10 ml of phosphoric acid (sp. gr. 1.698). The reaction was accompanied by the evolution of heat, the temperature rising to 44° by the time all the carbinol had been added. Stirring was continued for another 3 hours after the carbinol had been added. The reaction mass was diluted with ether, washed with water, and then washed several times with a 10% solution of sodium hydroxide to extract the acid reaction products.

The alkaline extracts were combined, acidulated with dilute hydrochloric acid, and extracted with ether, the ether solution being dried with magnesium sulfate, the ether driven off, and the remaining acid products distilled in vacuo. This yielded 2.7 g of the unreacted phenol (b.p. 55-58° at 3 mm) and 5.5 g of a diene phenol (IV) with a b.p. of 122-127° at 2.5 mm. The polymer residue totaled 4 g. The ether solution, which contained neutral products, was fractionated, yielding 1.6 g of a substance with a b.p. of 95-135°; n_D^{20} 1.536. The polymer residue totaled 1.8 g.

The diene phenol (IV) distilled without decomposition at 122-124° and 2.5 mm, solidified into a hard crystalline mass, and fused at 48.5-50°. It was soluble in alkalies, alcohol, ether, acetone, and benzene. It underwent no change in storage.

3.725 mg substance: 11.290 mg CO_2; 2.870 mg H_2O. 5.805 mg substance; 17.595 mg CO_2; 4.475 mg H_2O. Found %: C 82.71, 82.72; H 8.62, 8.62. $C_{13}H_{16}O$. Calculated %: C 82.97; H 8.51.

Condensation of the diene phenol (IV) with benzoyl chloride. 1 gram of the diene phenol (IV) was dissolved in 10 ml of 10% sodium hydroxide, and 2 g of benzoyl chloride was added gradually. An oily substance settled out, which crystallized the next day; the crystals were filtered out and recrystallized from alcohol. This yielded 0.55 g of a benzoyl derivative of the diene phenol (VIII) as white crystals with a m.p. of 81-82.5°.

8.83 mg substance: 26.39 mg CO_2; 5.49 mg H_2O. 10.56 mg substance: 31.65 mg CO_2; 6.94 mg H_2O. Found %: C 81.56, 81.79; H 6.96, 6.94. $C_{20}H_{20}O_2$. Calculated %: C 82.19; H 6.84.

Methylating the diene phenol (IV) with dimethyl sulfate. 7 grams of the diene phenol (IV) was dissolved in 50 ml of 10% sodium hydroxide, and 12 ml of dimethyl sulfate was gradually added. The mixture was agitated for half an hour; heat was evolved during the reaction.. Then a solution of sodium hydroxide was added until the reaction was alkaline, and the liquid was heated to the boiling point. After the liquid had cooled, the product was extracted with ether, dried with potash, and distilled in vacuo. This yielded 2.5 g of the methyl ether of the dien phenol (IX) as a colorless, transparent liquid with a b.p. of 153-156° at 5 mm.

n_D^{19} 1.5490; d_4^{19} 0.9582; MR_D found 64.04; calculated 63.84.

10.70 mg substance: 32.52 mg CO_2; 9.02 mg H_2O. 15.74 mg substance: 47.96 mg CO_2; 13.09 mg H_2O
Found %: C 82.94, 83.14; H 9.43, 9.25. $C_{14}H_{18}O$. Calculated %: C 83.16, H 8.91.

Hydrogenating the diene phenol (IV). When 3 g of the substance, dissolved in 50 ml of diethyl ether, was hydrogenated with a platinum catalyst prepared by the Adams method, 775 ml of hydrogen was absorbed (the theory calling for 784 ml of hydrogen). The catalyst was filtered out, the alcohol driven off, and the product distilled in vacuo. This yielded 2.4 g of p-isoheptylphenol (VI), with a b.p. of 282-283° at 746 mm; n_D^{20} 1.505.

5.035 mg substance: 14.920 mg CO_2; 4.765 mg H_2O. 4.560 mg substance: 13.525 mg CO_2; 4.310 mg H_2O.
Found %: C 81.04, 80.94; H 10.61, 10.58. $C_{13}H_{20}O$. Calculated %: C 81.25; H 10.42.

Condensing p-isoheptylphenol (VI) with benzoyl chloride. 1 gram of p-isoheptylphenol (VI) was dissolved in 10 ml of 10% sodium hydroxide, and 2 g of benzoyl chloride was added gradually. An oily substance settled out, which crystallized when the mixture was chilled with a freezing mixture (ice + salt). The filtered-out crystals were recrystallized from alcohol, yielding 0.5 g of the benzoyl derivative of p-isoheptylphenol (VII), with a m.p. of 31-33°.

5.190 mg substance: 15.439 mg CO_2; 3.936 mg H_2O. 6.695 mg substance: 19.919 mg CO_2; 5.140 mg H_2O.
Found %: C 81.18, 81.20; H 8.50, 8.58. $C_{20}H_{24}O_2$. Calculated %: C 81.03; H 8.16.

Oxidizing the methyl ether of the diene phenol (IX) with permanganate. 1.7 g of the substance was placed in a solution of 0.4 g of potash in 100 ml of water. Then 6.8 g of pulverized potassium permanganate was gradually added to the resulting mixture, with vigorous stirring and cooling with ice water (the temperature of the mixture did not rise above 1°). Oxidation lasted 12 hours. The manganese dioxide was filtered out and washed several times with hot water. 160 ml of water was driven off together with the volatile neutral products from the 250 ml of the combined filtrate. The distillate displayed a positive iodoform reaction. The distillate was saturated with potash while chilled with ice water, and another 60 ml of liquid was driven off from it. The distillate was resaturated with potash, and another 20 ml of liquid was driven off and saturated with potash, after which 6 ml more of a liquid with the obvious odor of acetone was driven off from the latter. The 2,4-dinitrophenylhydrazone prepared from this distillate had a m.p. of 124-126° after recrystallization from ethyl alcohol. Its mixed melting point with the known 2,4-dinitrophenylhydrazone of acetone exhibited no depression.

The residue left after the neutral products had been driven off was acidulated with hydrochloric acid. The crystals were filtered out, washed several times with water, and dried in a desiccator. This yielded 0.55 g of p-methoxybenzoic acid, which had a m.p. of 179-181° after recrystallization from water. Its mixed melting point with known p-methoxybenzoic acid exhibited no depression. After the crystals of p-methoxybenzoic acid had been filtered out, the filtrate was neutralized with ammonia and heated to a boil, a hot solution of calcium chloride being added to this solution while hot. Crystals of calcium oxalate, which decolorized permanganate, settled out.

Condensing dimethylbutylcarbinol with phenol in the presence of phosphoric acid. 70 grams of dimethylbutylcarbinol (b.p. 140-142°) was added drop by drop with constant stirring at a temperature of 65° to a mixture of 54 g of phenol and 27 ml of phosphoric acid (sp. gr. 1.82). The mixture was stirred for 17 hours at 80-90°. After it had cooled, the product was extracted with ether, and the ether solution was washed with water and then repeatedly with a 10% solution of sodium hydroxide to extract the acid reaction products.

The alkaline solutions were combined and acidulated with dilute hydrochloric acid and the product was extracted with ether. The ether solution was dried with potash, the ether was driven off, and the remaining acid products were distilled at atmospheric pressure. This yielded the following fractions: I — b.p. 178-180°, 28 g (phenol); II — b.p. 268-272°, 13 g; n_D^{20} 1.5149; tarry residue – 2 g. Redistillation of Fraction II yielded 10.5 g of the dimethylbutyl-p-hydroxyphenylmethane (XII) described previously, as a slightly yellowish liquid with the odor of phenol, b.p. 270-272°.

n_D^{20} 1.5155; d_4^{20} 0.9522; MR_D found 59.83; calculated 60.085.

3.861 mg substance: 14.425 mg CO_2; 3.615 mg H_2O. 3.785 mg substance: 11.205 mg CO_2; 3.575 mg H_2O.
Found %: C 80.75, 80.79; H 10.68, 10.56. $C_{13}H_{20}O$. Calculated %: C 81.25; H 10.42.

The ether solution containing the neutral products yielded 16 g of 2-methyl-2-hexene (b.p. 93-95°; n_D^{19} 1.413). produced by the dehydration of the dimethylbutylcarbinol. The neutral products also yielded 16 g of a mixture of high-boiling products (b.p. 70-148°; n_D^{19} 1.505), which was not investigated further.

Methylating dimethylbutyl-p-hydroxyphenylmethane (XII) with dimethyl sulfate. 5 grams of the substituted phenol (XII) was dissolved in 25 ml of 10% sodium hydroxide, and 8 ml of dimethyl sulfate was added gradually. The mixture was agitated for half an hour (heat was evolved during the reaction), and then a solution of sodium hydroxide was added until the reaction was alkaline, and the liquid was heated to a boil. After it had cooled, the product was extracted with ether, dried with potash, and fractionated in vacuo. This yielded 2.5 g of the methyl ether (XIV) with a b.p. of 104-105° at 3 mm.

n_D^{20} 1.5020; d_4^{20} 0.9349; MR_D found 64.97; calculated 64.78.

3.045 mg substance: 9.054 mg CO_2; 2.960 mg H_2O. 7.214 mg substance: 21.489 mg CO_2; 6.915 mg H_2O. Found %: C 81.14, 81.30; H 10.85, 10.70. $C_{14}H_{22}O$. Calculated %: C 81.55; H 10.67.

Condensing dimethylbutyl-p-hydroxyphenylmethane (XII) with benzoyl chloride. 1 g of the substituted phenol (XII) was dissolved in 10 ml of 10% sodium hydroxide, and 2 g of benzoyl chloride was slowly added. An oil settled out, which crystallized the next day. The crystals were filtered out and recrystallized from alcohol. This yielded 0.7 g of the benzoyl derivative (XIII) described previously, with a m.p. of 42-43°.

11.45 mg substance: 34.01 mg CO_2; 8.51 mg H_2O. 11.33 mg substance: 33.79 mg CO_2; 8.39 mg H_2O. Found %: C 81.06, 81.30; H 8.35, 8.24. $C_{20}H_{24}O_2$. Calculated %: C 81.03; H 8.16.

SUMMARY

The condensation of 5-methyl-1,3-hexadien-5-ol (II) with phenol in the presence of phosphoric acid involves a rearrangement, in which a para-substituted diene phenol (IV) is produced, corresponding to the primary diene alcohol (III).

Methylating the diene phenol (IV) with dimethyl sulfate yields a methyl ether (IX), oxidation of which with permanganate yields anisic acid, oxalic acid, and acetone. Two molecules of hydrogen are absorbed when the diene phenol (IV) is hydrogenated catalytically, p-isoheptylphenol (VI) being produced.

It is much harder to condense 5-methylhexan-5-ol (XI) with phenol in the presence of phosphoric acid, the normal condensation product — the tertiary para-substituted phenol (XII) — being formed. Benzoylating the phenols (IV, VI, and XII) with benzoyl chloride yielded the respective crystalline benzoates.

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Received June 2, 1950

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DERIVATIVES OF ACETYLENE

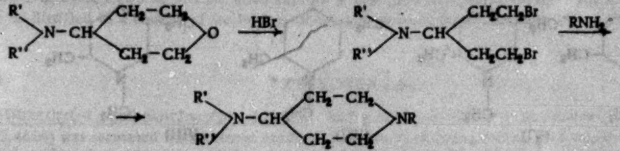
137. HETEROCYCLIC COMPOUNDS

XIII. THE REACTION OF 4-PIPERIDONES WITH PRIMARY AMINES.

SYNTHESIS OF 4-IMINO- AND 4-AMINOPIPERIDINES

I.N. Nazarov and V.A. Rudenko

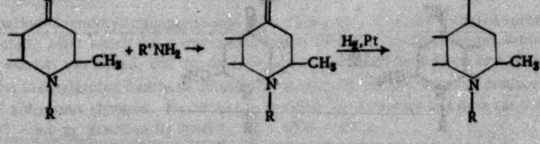
Among the numerous papers on the synthesis and investigation of amines that possess spasmolytic action the researches on the substitution derivatives of 4-aminopiperidines occupy an important place. Most of the compounds of this group, which mainly contain a tertiary amino group, were synthesized by Hahn, Cerkovnikov, and Prelog [1] by reacting the primary amines with 1,5-dibromo-3-aminopentanes, which were produced in turn by reacting fuming hydrobromic acid with the respective 4-aminotetrahydropyrans:



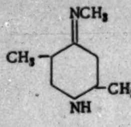
Some of the synthesized compounds of this series exhibit greater spasmolytic action than papaverine. But the complexities of the synthesis, particularly of the members containing an amino group, greatly limit the possibilities of investigating this interesting series of amines.

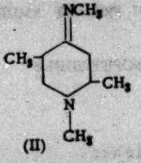
In our preceding paper [2], which described a new method of synthesizing the substituted γ-piperidones by reacting vinyl allyl ketones with ammonia and primary amines, we noted that in several instances the analysis of the synthesized γ-piperidones indicated an excessively high percentage of nitrogen, whereas analysis of the picrates of these piperidones yielded the theoretical results. This circumstance compelled us to assume that the excessively high percentage of nitrogen in some of the γ-piperidones, synthesized by the action of an excess of methylamine on the vinyl allyl ketones, is due to traces of 4-methylaminopiperidines, products of the reaction of the γ-piperidones with monomethylamine.

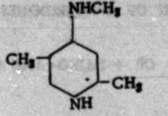
The present research had as its objectives proving that 4-methyliminopiperidines were present in the products of the reaction between substitution derivatives of vinyl allyl ketone and monomethylamine (when the latter is present in considerable excess) and synthesizing 4-iminopiperidines by reacting various primary amines with the γ-piperidones, which would make it possible to effect the transition to the 4-aminopiperidines, i.e. to a series of substances that exhibit spasmolytic activity. We found that when the γ-piperidones were heated on a water bath with primary amines (methylamine, ethylamine, and aniline), the readily hydrolyzable 4-iminopiperidines were actually produced, their hydrogenation yielding the respective 4-aminopiperidines:

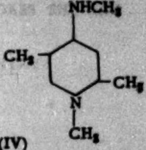


When monomethylamine is heated in a metalic ampoule with 2,5-dimethyl-4-piperidone or 1,2,5-trimethyl-4-piperidone, we get 2,5-dimethyl-4-methyliminopiperidine (I) and 1,2,5-trimethyl-4-methyliminopiperidine (II), respectively, neither of which could be easily isolated in the pure state. But the respective hydrogenated products — 2,5-dimethyl-4-methylaminopiperidine (III) and 1,2,5-trimethyl-4-methylaminopiperidine (IV) — could be readily recovered in the pure state by hydrogenating the major fractions over a Pt catalyst in both instances:


(I)

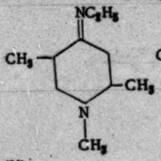

(II)

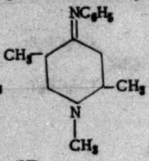

(III)

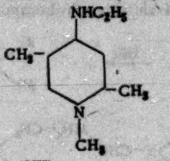

(IV)

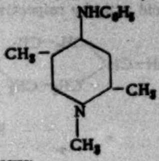
When 1,2,5-trimethyl-4-piperidone was heated with ethylamine and aniline, distillation in vacuo readily yielded 1,2,5-trimethyl-4-ethyliminopiperidine (V) and 1,2,5-trimethyl-4-phenyliminopiperidine (VI) in the pure state.

Hydrogenating 1,2,5-trimethyl-4-ethyliminopiperidine (V) in alcohol over a Pt catalyst converted it into 1,2,5-trimethyl-4-ethylaminopiperidine (VII). 1,2,5-Trimethyl-4-phenyliminopiperidine (VI) is hydrogenated over a Pt catalyst very slowly; adding palladium and nickel catalysts did not speed up hydrogenation. The 1,2,5-trimethyl-4-phenyliminopiperidine was reduced by reacting an alcoholic solution of the imino compound with metallic sodium. Distillation of the reduction product in vacuo yielded 1,2,5-trimethyl-4-phenylaminopiperidine (VIII):

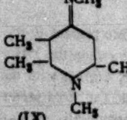

(V)

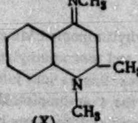

(VI)

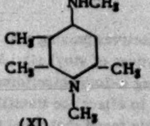

(VII)

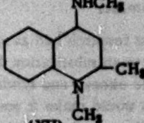

(VIII)

Heating 1,2,3,6-tetramethyl-4-piperidone (XIII) and 1,2-dimethyl-4-ketodecahydroquinoline (XVII) on a water bath with monomethylamine, followed by fractionation of the reaction products in vacuo yielded 1,2,3,6-tetramethyl-4-methyliminopiperidine (IX) and 1,2-dimethyl-4-methyliminodecahydroquinoline (X). The results of our analysis for the percent of nitrogen in the resultant preparations (IX) and (X)proved to be somewhat low, owing to the proximity of the boiling points of the synthesized imino compounds to those of the initial piperidones. Reducing these compounds with hydrogen over a Pt catalyst in alcoholic solution, however, yielded the analytically pure 1,2,3,6-tetramethyl-4-methylaminopiperidine (XI) and 1,2-dimethyl-4-methylaminodecahydroquinoline (XII):

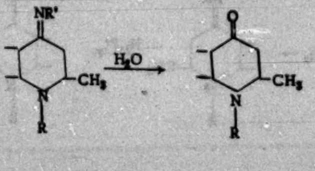

(IX)


(X)

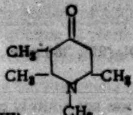

(XI)

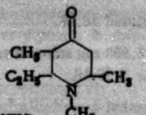

(XII)

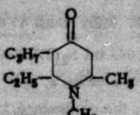
When all the 4-iminopiperidines described in this paper were heated with water or dilute hydrochloric acid, they were completely hydrolyzed into the respective γ-piperidones:

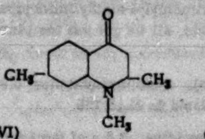


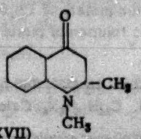
Thus, the γ-piperidones can be readily freed of any traces of the respective 4-iminopiperidines they may contain, as has been shown in the 1,2,3,6-tetramethyl-4-piperidone (XIII), the 1,2,5-trimethyl-6-ethyl-4-piperidone (XIV), the 1,2-dimethyl-6-ethyl-5-propyl-4-piperidone (XV), the 1,2,7-trimethyl-4-ketodecahydroquinoline (XVI), and the 1,2-dimethyl-4-ketodecahydroquinoline (XVII), which were previously synthesized by reacting the corresponding derivatives of vinyl allyl ketone with an excess of methylamine and contained appreciable quantities of 4-imino derivatives as impurities.


(XIII)


(XIV)


(XV)


(XVI)


(XVII)

The 4-iminopiperidines are mobile liquids with the strong unpleasant odors of bases. They quickly turn yellow when allowed to stand, and tar when kept for a long time exposed to the air. The 4-iminopiperidines should be distilled in a current of well-dried nitrogen because of their instability and tendency to hydrolyze.

EXPERIMENTAL

2,5-Dimethyl-4-methylaminopiperidine (III). 26.5 g of 2,5-dimethyl-4-piperidone (b.p. 71-73° at 8 mm; n_D^{19} 1.4650) was saturated with gaseous methylamine, the flask being chilled with an ice-salt mixture, after which 6.6 g of methylamine was added, and the mixture was heated for 6 hours in a metal ampoule to 90-95°. After heating was over, the reaction product was distilled in vacuo in a current of anhydrous nitrogen. After a small head fraction (1.6 g), containing water and the initial piperidone, had been driven off, we secured 21 g of a mixture of the initial piperidone and 2,5-dimethyl-4-iminopiperidine (I), b.p. 78-81° at 10 mm; n_D^{20} 1.4780. In view of the fact that it was impossible to separate this mixture by fractionation in vacuo, it was hydrogenated catalytically with a platinum catalyst in a solution of 40 ml of ethyl alcohol. Only after 6 hours had elapsed did the absorption of hydrogen set in; it continued for 15 hours, 2280 ml of hydrogen being absorbed. The alcohol was driven off, and the hydrogenation product was repeatedly fractionated in vacuo. This yielded 4.5 g of pure 2,5-dimethyl-4-methylaminopiperidine (III) with a b.p. of 67° at 7.5 mm:

n_D^{20} 1.4720; d_4^{20} 0.9043. MR_D found 44.15; calculated 44.05.

3.345 mg substance: 8.260 mg CO_2; 3.780 mg H_2O. 5.195 mg substance: 12.868 mg CO_2; 5.941 mg H_2O. 3.817 mg substance: 0.655 ml N_2 (25°, 743 mm). 4.730 mg substance: 0.792 ml N_2 (24°, 757 mm). Found %: C 67.39, 67.57; H 12.64, 12.80; N 19.22, 19.17. $C_8H_{18}N_2$. Calculated %: C 67.55; H 12.76; N 19.69.

The picrate of 2,5-dimethyl-4-methylaminopiperidine, prepared by mixing the base with an alcoholic solution of picric acid, had a m.p. of 220° (from alcohol).

In addition to the 2,5-dimethyl-4-methylaminopiperidine, this experiment yielded 12 g of a crystalline mixture of the isomeric 2,5-dimethyl-4-hydroxypiperidines (m.p. 68-110°), produced by the catalytic reduction of the carbonyl group in 2,5-dimethyl-4-piperidone.

1,2,5-Trimethyl-4-methyliminopiperidine (II). 13.4 g of 1,2,5-trimethyl-4-piperidone (b.p. 70-72° at 8 mm; n_D^{21} 1.4582), after which 6.6 g methylamine was chilled (ice-salt mixture), saturated with gaseous methylamine (125% excess) was added, and the mixture heated to 70-75° for 4 hours in a metal ampoule on a water bath. After the excess methylamine had been driven off, the faintly colored reaction product was distilled in vacuo in a current of anhydrous nitrogen. Fractionation yielded the following fractions (at 8 mm): Fraction I) 76-78°; n_D^{21} 1.4697 – 9.0 g; Fraction II) 78-80°; n_D^{21} 1.4732 – 3.7 g.

The first fraction was again saturated with gaseous methylamine under the same conditions as before and heated to 75° for 4 hours. The reaction product secured after vacuum fractionation in a current of nitrogen totaled 5.5 g (b.p. 78-80° at 8 mm; n_D^{21} 1.4746); it was combined with Fraction II, and the whole was then redistilled in vacuo (at 8 mm) in a current of anhydrous nitrogen: Fraction I — 76-78°; n_D^{20} 1.4748, 5.3 g; and Fraction II — 78-80°; n_D^{20} 1.4752, 3.8 g.

Fraction II was 1,2,5-trimethyl-4-methyliminopiperidine (II), a colorless liquid that rapidly turned yellow upon standing. B.p. 78-80° at 8 mm.

n_D^{20} 1.4752; d_4^{20} 0.9118. MR_D Found 47.65; calculated 48.18.

7.025 mg substance: 1.045 ml N_2 (22°, 749 mm). 5.990 mg substance: 0.885 ml N_2 (22°, 750 mm).
Found %: N 16.96, 16.87. $C_9H_{18}N_2$. Calculated %: N 18.16.

As the analysis showed, the synthesized 1,2,5-trimethyl-4-methyliminopiperidine was not entirely pure, containing a slight trace of 1,2,5-trimethyl-4-piperidone.

When we tried to secure the picrate of 1,2,5-trimethyl-4-methyliminopiperidine by reacting the reaction product with a saturated alcoholic solution pf picric acid, all we got was the picrate of 1 2 5-trimethyl-4-piperidone, m.p. 161-162° from alcohol.

4.415 mg substance: 0.583 ml N_2 (23°, 749 mm). 4.640 mg substance: 0.613 ml N_2 (23°, 750 mm).
Found %: N 15.01, 15.04. $C_{14}H_{18}O_8N_4$. Calculated %: N 15.135.

Hydrolysis of 1,2,5-trimethyl-4-methyliminopiperidine. 3.5 g of the 1,2,5-trimethyl-4-methyliminopiperidine (b.p. 78-80° at 8 mm; n_D^{20} 1.4752) described above was dissolved in 40 ml of water, and the solution was allowed to stand at room temperature for 20 hours, after which it was heated to 80-90° for 4.5 hours. After having been salted out with potash, the hydrolysis product was extracted with ether, dried with potash, and distilled in vacuo. This yielded 2.3 g of 1,2,5-trimethyl-4-piperidone with a b.p. of 74-75° at 8 mm; n_D^{12} 1.4615. Its picrate had a m.p. of 161° and exhibited no depression when mixed with the picrate of known 1,2,5-trimethyl-4-piperidone.

1,2,5-Trimethyl-4-methylaminopiperidine (IV). 5.3 g of 1,2,5 trimethyl-4-methyliminopiperidine (b.p. 76-78° at 8 mm; n_D^{20} 1.4748) was hydrogenated in 10 ml of absolute alcohol with a platinum catalyst. The absorption of hydrogen set in only after 3.5 hours had elapsed and lasted 40 minutes, 820 ml of hydrogen being absorbed.

After the catalyst had been filtered out and the solvent had been driven off, the hydrogenated product was fractionated in vacuo (at 8 mm): Fraction I) 74-76°; n_D^{18} 1.4592 — 0.9 g; Fraction II) 76-81°; n_D^{18} 1.4652 — 3.3 g.

Double distillation of the latter fraction in vacuo yielded 1.9 g of pure 1,2,5-trimethyl-4-methylaminopiperidine (IV) as a colorless liquid with a strong amine odor, b.p. 72-73° at 7 mm:

n_D^{20} 1.4637; d_4^{20} 0.8828. MR_D found 48.97; calculated 49.10.

3.975 mg substance: 10.030 mg CO_2; 4.530 mg H_2O. 4.280 mg substance: 10.810 mg CO_2; 4.870 mg H_2O.
Found %: C 68.86, 68.93; H 12.75, 12.73. $C_9H_{20}N_2$. Calculated %: C 69.17; H 12.90.

Picrate: m.p. 234-235° (from 50% alcohol).

1,2,5-Trimethyl-4-ethyliminopiperidine (V). 10.6 g of 1,2,5-trimethyl-4-piperidone (b.p. 70-72° at 8 mm; n_D^{21} 1.4582) was mixed with 7.4 g of ethylamine (approximately 120% excess), and the mixture was heated to 65-70° for 3 hours in a steel ampoule. The light-yellow reaction product was dried with potash, the excess ethylamine was driven off, and the residue was vacuum-fractionated in a current of anhydrous nitrogen. This yielded 9 g of 1,2,5-trimethyl-4-ethyliminopiperidine (V) as a mobile, colorless liquid with the strong odor of pyridine bases. M.p. 82-83.5° at 8 mm.

n_D^{20} 1.4690; d_4^{20} 0.8915. MR_D found 52.57; calculated 52.80.

8.195 mg substance: 1.176 ml N_2 (21°, 754 mm). 5.208 mg substance: 0.766 ml N_2 (23°, 739 mm).
Found %: N 16.53, 16.49. $C_{10}H_{20}N_2$. Calculated %: N 16.65.

1,2,5-Trimethyl-4-ethylaminopiperidine (VII). 8.3 g of the 1,2,5-trimethyl-4-ethyliminopiperidine described above was dissolved in 10 ml of absolute alcohol and reduced with hydrogen and a platinum catalyst. Hydrogen was absorbed very slowly during the first 15-20 minutes, after which it sped up considerably, 1200 ml of hydrogen being absorbed during 1.5 hours. After hydrogenation slowed down sharply, some more catalyst was added, and hydrogenation was continued for another hour. After the catalyst had been filtered out and the alcohol driven off the hydrogenation product was distilled in vacuo. This yielded 5 g of 1,2,5-trimethyl-4-ethylaminopiperidine

(VII) as a colorless liquid with a strong amine odor. B.p. 83-84° at 9 mm.

n_D^{20} 1.4604; d_4^{20} 0.8732: MR_D found 53.45; calculated 53.72.

4.964 mg substance: 12.580 mg CO_2; 5.785 mg H_2O. 3.520 mg substance: 9.115 mg CO_2; 4.140 mg H_2O. Found %: C 70.77, 70.67; H 13.10, 13.15. $C_{10}H_{22}N_2$. Calculated %: C 70.53; H 13.02.

The picrate of 1,2,5-trimethyl-4-ethylaminopiperidine was produced as soon as the base was added to an alcoholic solution of picric acid. It is very poorly soluble in hot alcohol. The m.p. of the picrate was 218° after double recrystallization from 50% alcohol.

1,2,5-Trimethyl-4-phenyliminopiperidine (VI). A mixture of 25 g of 1,2,5-trimethyl-4-piperidone and 25 g of aniline was heated to 85-90° on a water bath for 4.5 hours. Then the mixture was heated in a 100-mm vacuum for 3 hours, about 1 g of water being driven off. Vacuum fractionation of the reaction products in a current of anhydrous nitrogen yielded 37 g of a mixture of the unreacted aniline and piperidone (b.p. 75-78° at 10 mm) plus 7.5 g of 1,2,5-trimethyl-4- phenyliminopiperidine (VI) with a b.p. of 131-132° at 5 mm.

n_D^{20} 1.5432; d_4^{20} 0.9892. MR_D found 68.95; calculated 67.67.

10.064 mg substance: 1.150 ml N_2 (24°, 752 mm). 9.600 mg substance: 1.091 ml N_2 (22°, 751 mm). Found %: N 12.99, 13.00. $C_{14}H_{20}N_2$. Calculated %: N 12.95.

When we tried to secure the picrate by reacting the reaction product with an alcoholic solution of picric acid we got the picrate of 1,2,5-trimethylpiperidone, with a m.p. of 159-161°, which exhibited no depression when mixed with a known sample.

The synthesized 1,2,5-trimethyl-4- phenyliminopiperidine is hardly hydrogenated at all with Pt, Pd, and Ni catalysts. We therefore effected hydrogenation with metallic sodium in an absolute alcohol solution.

1,2,5-Trimethyl-4-phenylaminopiperidine (VIII). 5 grams of 1,2,5-trimethyl-4 - phenyliminopiperidine was dissolved in 80 ml of alcohol, and 8 g of metallic sodium was added in small bits to the continuously stirred solution. After all the sodium had dissolved, the solution was neutralized with 70 ml of dilute hydrochloric acid (1:1), the precipitated sodium chloride being filtered out and the alcohol driven off, while alkali was added to the aqueous solution of the amine hydrochloride until the free base separated as a separate layer. The free base was extracted with ether, dried with a caustic alkali, and fractionated in vacuo. This yielded 3 g of 1,2,5-trimethyl-4-phenylaminopiperidine (VIII) as a viscous, thick, colorless oil with a faint amine odor. B.p. 138-139° at 4 mm; 150-151° at 6.5 mm.

n_D^{20} 1.5472; d_4^{20} 0.9668· MR_D found 71.64. Calculated 68.59.

3.597 mg substance: 10.065 mg CO_2; 3.270 mg H_2O. 6.605 mg substance: 18.450 mg CO_2; 5.945 mg H_2O. Found %: C 76.35, 76.23; H 10.17, 10.07. $C_{14}H_{22}N_2$. Calculated %: C 77.01; H 10.16.

1,2,3,6-Tetramethyl-4-piperidone (XIII). 40 g of the 1,2,3,6-tetramethyl-4-piperidone described previously [2], prepared by reacting methylamine with 5-methyl-1,5-heptadien-4-one and therefore containing 1,2,3,6-tetramethyl-4-methyliminopiperidine as an impurity, was dissolved in 200 ml of water, and the solution was refluxed at 80-90° for 5 hours. Heating results in the partial separation of the piperidone as a layer, which redissolves as the reaction mixture cools. After salting out with potash, the product was extracted with ether, dried with calcined potash, and fractionated in vacuo. This yielded 34.8 g of pure 1,2,3,6-tetramethyl-4-piperidone (XIII) with a b.p. of 86-88° at 7.5 mm.

n_D^{20} 1.4680; d_4^{20} 0.9499. MR_D found 45.43; calculated 45.51.

9.337 mg substance; 0.746 ml N_2 (24°, 733 mm). 6.445 mg substance: 0.529 ml N_2 (25°, 733 mm). Found %: N 8.86, 9.07. $C_9H_{17}ON$. Calculated %: N 9.02.

1,2,3,6-Tetramethyl-4-methyliminopiperidine (IX). We took 30 g of 1,2,3,6-tetramethyl-4-piperidone (b.p. 86-88° at 7.5. mm; n_D^{20} 1.4680), chilled it with ice and salt, and then dissolved 11.5 g of gaseous methylamine (a 90% excess) in it. The mixture was then heated to 90° in a metallic ampoule for 4.5 hours. After the excess methylamine had been driven off and the overhead fractions, consisting mainly of water (2.1 g) had been distilled, distillation in a current of anhydrous nitrogen yielded 29.5 g of a product with a b.p. of 90.5-93° at 7.5 mm; n_D^{19} 1.4800. Triple distillation in vacuo in a current of anhydrous nitrogen yielded 11.5 g of 1,2,3,6-tetramethyl-4-methyliminopiperidine (IX) as a colorless mobile liquid with the disagreeable strong odor of a base. B.p. 90-91° at 7.5 mm.

n_D^{20} 1.4818; d_4^{20} 0.9140. MR_D found 52.47; calculated 52.80.

5.680 mg substance: 0.794 ml N_2 (22°, 749 mm). 5.470 mg substance: 0.761 ml N_2 (21°, 750 mm).
Found %: N 15.94, 15.94. $C_{10}H_{20}N_2$. Calculated %: N 16.65.

When we tried to secure the picrate by using an alcoholic solution of picric acid, we got the picrate of 1,2,3,6-tetramethylpiperidone, with a m.p. of 146-148°, which exhibited no depression when mixed with a known sample.

1,2,3,6-Tetramethyl-4-methylaminopiperidine (XI). 5.2 grams of 1,2,3,6-tetramethyl-4-methyliminopiperidine (b.p. 90-91° at 7.5 mm; n_D^{20} 1.4818) was dissolved in 12 ml of alcohol, and the solution was agitated in hydrogen under pressure with a platinum catalyst. It took 3 hours for the absorption of hydrogen to start, the hydrogen absorbed totalling 740 ml. The catalyst was filtered out, the solvent driven off, and the hydrogenation product distilled twice in vacuo. This yielded 2.5 g of 1,2,3,6-tetramethyl-4-methylaminopiperidine (XI) as a colorless liquid with the odor of a base. B.p. 76-77° at 4.5 mm.

n_D^{25} 1.4720; d_4^{25} 0.8971. MR_D found 53.16; calculated 53.72.

3.263 mg substance: 8.450 mg CO_2; 3.795 mg H_2O. 4.950 mg substance: 12.796 mg CO_2; 5.730 mg H_2O.
Found %: C 70.67, 70.51; H 13.10, 12.95. $C_{10}H_{22}N_2$. Calculated %: C 70.53; H 13.02.

The dipicrate of 1,2,3,6-tetramethyl-4-methylaminopiperidine was slightly soluble in alcohol. M.p. 232-233° with decomposition (from 50% alcohol).

6.145 mg substance: 9.445 mg CO_2; 2.435 mg H_2O. 4.296 mg substance: 6.580 mg CO_2; 1.685 mg H_2O.
4.765 mg substance: 0.756 ml N_2 (23°, 729 mm). 4.410 mg substance: 0.696 ml N_2 (23°, 730 mm).
Found %: C 41.94, 41.80; H 4.41, 4.39; N 17.55, 17.48. $C_{22}H_{28}O_{14}N_8$. Calculated %: C 42.04; H 4.49; N 17.83.

1,2-Dimethyl-4-ketodecahydroquinoline (XVII). The preparation of 1,2-dimethyl-4-ketodecahydroquinoline prepared with a great excess of methylamine (sevenfold excess), which grew very dark when stored for a long time (2 years) and turned into a thick black mass, was double-distilled again in vacuo. Distillation yielded 3.0 g of pure 1,2-dimethyl-4-ketodecahydroquinoline (XVII) as a colorless liquid that was stable in storage, with a b.p. of 111-112° at 5 mm.

n_D^{20} 1.4970; d_4^{20} 1.0111. MR_D found 52.46; calculated 52.55.

4.440 mg substance: 0.303 ml N_2 (23°, 723 mm). 3.410 mg substance: 0.239 ml N_2 (23°, 723 mm).
Found %: N 7.49, 7.69. $C_{11}H_{19}ON$. Calculated %: N 7.77.

1,2-Dimethyl-4-methyliminodecahydroquinoline (X). 14 grams of 1,2-dimethyl-4-keotodecahydroquinoline (b.p. 111-112° at 5 mm) was chilled with an ice-salt mixture, after which it dissolved 6.7 g of gaseous methylamine (some 200% excess). The solution was heated to 80-90° in a metallic ampoule for 6 hours. Double fractionation of the reaction product in vacuo in a current of nitrogen yielded 2.5 g of 1,2-dimethyl-4-methyliminodecahydroquinoline (X), with a b.p. of 112-113° at 4 mm.

n_D^{20} 1.5095; d_4^{20} 0.9809. MR found 59.20; calculated 58.83.

5.290 mg substance: 0.588 ml N_2 (23°, 761 mm). 7.195 mg substance: 0.794 ml N_2 (23°, 761 mm).
Found %: N 12.84, 12.74. $C_{12}H_{22}N_2$. Calculated %: N 14.42.

Analysis showed that the synthesized 1,2-dimethyl-4-methyliminodecahydroquinoline was not wholly pure, containing a trace of the initial 1,2-dimethyl-4-ketodecahydroquinoline.

When 1,2-dimethyl-4-methyliminodecahydroquinoline was mixed with an alcoholic solution of picric acid, the picrate was formed at once, settling out as an oil and crystallizing when the solution was heated. When the picrate was recrystallized from alcohol, part of it remained undissolved and was set aside. The picrate crystals that settled out of the solution had an m.p. of 158° and exhibited no depression when mixed with the previously prepared picrate of 1,2-dimethyl-4-ketodecahydroquinoline (m.p. 157-157.5°).

The slightly soluble picrate was recrystallized, after which its melting point was 174-175°; its composition was likewise that of the picrate of 1,2-dimethyl-4-ketodecahydroquinoline.

4.370 mg substance: 0.490 ml N_2 (22°, 752 mm). 5.677 mg substance: 0.642 ml N_2 (22°, 752 mm).
Found %: N 12.84, 12.95. $C_{17}H_{22}O_8N_4$. Calculated %: N 13.69.

1,2 -Dimethyl-4-methylaminodecahydroquinoline (XII). 7 grams of 1,2-dimethyl-4-methyliminodecahydroquinoline was dissolved in 15 ml of alcohol, and the solution was agitated with a platinum catalyst in hydrogen under pressure. Hydrogen began to be absorbed after 2 hours had passed, being slow at first, but later speeding up considerably. A total of 840 ml of hydrogen was absorbed in 40 minutes. The catalyst was then filtered out, the solvent driven off, and the reaction product fractionated in vacuo. This yielded 4.0 g of 1,2-dimethyl-4-methylaminodecahydroquinoline (XII) as a colorless liquid that rapidly turned pink in storage. B.p. 113-115° at 6.5 mm.

n_D^{21} 1.4985.

3.466 mg substance: 9.335 mg CO_2; 3,675 mg H_2O. 3.399 mg substance: 9.155 mg CO_2; 3.630 mg H_2O. Found %: C 73.50, 73.50; H 11.86, 11.95. $C_{12}H_{24}N_2$. Calculated %: C 73.41; H 12.33.

The dipicrate of 1,2-dimethyl-4-methylaminodecahydroquinoline settled out as an oil when the base was mixed with a saturated alcoholic solution of picric acid and slowly crystallized. Recrystallization from 50% alcohol yielded a picrate with an m.p. of 214-216° (turning dark at about 200°).

4.150 mg substance: 0.613 ml N_2 (22°, 752 mm). 4.542 mg substance: 0.679 ml N_2 (22°, 752 mm). Found %: N 16.91, 17.12. $C_{24}H_{30}O_{14}N_8$. Calculated %: N 17.12.

1,2,5-Trimethyl-6-ethyl-4-piperidone (XIV). 5 grams of the previously described [3] 1,2,5-trimethyl-6-ethyl-4-piperidone (b.p. 74-76° at 3 mm; n_D^{20} 1.4712, and b.p. 76-78°; 3 mm; n_D^{20} 1.4743), produced with a large excess of methylamine and containing 1,2,5-trimethyl-6-ethyl-4-methyliminopiperidine as an impurity, was mixed with 25 ml of water, and the mixture was vigorously stirred for 6 hours at 85-90°. After salting out with potash, the base was extracted with ether, dried with potash, and distilled in vacuo. Double distillation yielded 3.5 g of pure 1,2,5-trimethyl-6-ethyl-4-piperidone (XIV) as a colorless, mobile liquid with the odor of a base. B.p. 84.5-96° at 7 mm.

n_D^{20} 1.4682; d_4^{20} 0.9502. MR_D Found 49.54; Calculated 50.13.

6.730 mg substance: 0.509 ml N_2 (23°, 738 mm). 7.290 mg substance: 0.554 ml N_2 (23°, 738 mm). Found %: N 8.47, 8.51. $C_{10}H_{19}ON$. Calculated %: N 8.28.

1,2-Dimethyl-6-ethyl-5-propyl-4-piperidone (XV). 6 grams of the previously described [2] 1,2-dimethyl-6-ethyl-5-propyl-4-piperidone, synthesized with a large excess of methylamine and containing the imino derivative as an impurity (b.p. 81-83° at 2.5 mm; n_D^{20} 1.4682), was dissolved in 40 ml of 7% hydrochloric acid. The solution was heated for 5 hours to 80-90°, after which the base was recovered from the solution by adding a solid alkali, extracting with ether, and drying the ether solution with magnesium sulfate. After the ether had been driven off, the base was double-distilled in vacuo, yielding 5.1 g of pure 1,2-dimethyl-6-ethyl-5-propyl-4-piperidone (XV) as a colorless, mobile liquid with a b.p. of 122-124° at 13 mm.

n_D^{20} 1.4684; d_4^{20} 0.9285. MR_D found 59.12; calculated 59.37.

5.187 mg substance: 0.327 ml N_2 (23°, 755 mm). 7.580 mg substance: 0.474 ml N_2 (24°, 749 mm). Found %: N 7.22, 7.08. $C_{12}H_{23}ON$. Calculated %: N 7.10.

1,2,7-Trimethyl-4-ketodecahydroquinoline (XVI). 8 grams of the previously described [2] 1,2,7-trimethyl-4-ketodecahydroquinoline (b.p. 123.5° at 4 mm; n_D^{20} 1.4913), prepared with a large excess of methylamine and containing the imino derivative as an impurity, was dissolved in 50 ml of 7% hydrochloric acid, and the solution was heated to 85-90° for 6 hours. The free base was recovered by adding alkali, extracting with ether, drying with magnesium sulfate and double-distillation in vacuo. This yielded 4.4 g of pure 1,2,7-trimethyl-4-ketodecahydroquinoline (XVI) with a b.p. of 121-123° at 6 mm.

n_D^{20} 1.4927; d_4^{20} 0.9932. MR_D found 57.11; calculated 57.17.

3.305 mg substance: 0.220 ml N_2 (22°, 728 mm). 4.790 mg substance: 0.313 ml N_2 (22°, 733 mm). Found %: N 7.38, 7.29. $C_{12}H_{21}ON$. Calculated %: N 7.17.

SUMMARY

When γ-piperidones are heated with primary amines (methylamine, ethylamine, and aniline), the 4-iminopiperidines are produced: they are recovered in the pure state in some instances. When the 4-iminopiperidines are heated with water or dilute hydrochloric acid, they are readily hydrolyzed, yielding

the initial γ-piperidones, while hydrogenation converts them into the respective 4-aminopiperidines.

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Received June 2, 1950.

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CATALYTIC CONDENSATION OF ALCOHOLS WITH KETONES

I. CONDENSATION OF METHANOL WITH ACETONE

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There is an extensive literature on the condensation of ketones in the homogeneous phase, resulting in the formation of mesitylene, isophorone, xylitone, their analogs, their higher homologs, and other cyclic sybstances. No work has been done at all on the heterogeneous catalytic condensation of ketones. Nothing is known of the catalytic condensation of a mixture of alcohols and ketones in the heterogeneous phase. The only paper we have is one by Reckleben and Scheiber [1], who secured hexamethylbenzene from a mixture of methanol and acetone over alumina. Our endeavor to reproduce the results of these authors met with no success. No hexamethylbenzene was secured at all, the oily condensate layer containing appreciable quantities of phenols, which Reckleben and Scheiber did not secure. We assumed that so great a discrepancy in the course of the process must be due mainly to the nature of the catalyst. Subsequent experiments fully confirmed this assumption. The alumina we used, which came from the Central Chemical Supply Board, produced phenols at 400°, while the alumina supplied by the Kahlbaum firm yielded nothing but hexamethylbenzene (10 -12%) under the same conditions. At our request, both samples were analyzed in the X-ray laboratory of the Institute of Applied Chemistry. Traces of Na and Mg were found in both samples, the German sample also containing copper, while the native sample contained iron and silicon. Assuming that the formation of phenols was caused by the presence of iron, we added the latter to the German sample of Al_2O_3 and actually secured phenols instead of hexamethylbenzene. This process seemed to us to be worthy of further study, which we therefore undertook.

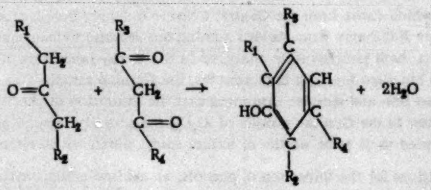
To determine the optimum conditions for the formation of phenols, an equimolecular mixture of methanol and acetone was passed over Al_2O_3 containing different percentages of iron at various temperatures and volumetric flow rates. The effect of the iron content was studied at 410 -420° and a rate of flow of 8 -8.5 ml of the initial mixture per hour The phenol yield proved to be a maximum above catalysts containing 10 -15% of iron, so that we chose an Al_2O_3 catalyst containing 10% Fe for all our subsequent research The following were found to be the conditions required for optimum phenols yields from a methanol-acetone mixture: an Al_2O_3 catalyst containing 10% Fe at 400 -410° and a flow rate of 8 -8.5 ml of the mixture per hour over 100 ml of the catalyst. This yielded a two-layer condensate, the upper, oily layer containing the phenols, while the lower one consisted mainly of a methanol-acetone mixture with other reaction products of a nonphenolic nature. The phenol yield totaled 6.5% of the initial mixture or 8.9% of the condensate. The yield of the neutral oil was 7.9% of the initial mixture and 10.8% of the condensate.

After the phenol layer had been separated, it was fractionated into a column with an efficiency of 25 theoretical trays, the phenols being identified in each fraction by the Steinkopf and Hopner [2] or the Holzman and Pilat method [3], involving their conversion into the respective aryl glycolic acids by means of monochloroacetic acid and solid sodium hydroxide. In some instances the production of the aryl glycolic acids was preceded by the separation of the phenols by the Bruckner method [4], involving the fractional cleavage of the phenolsulfonic acids We have isolated and identified the following phenols: phenol, m-cresol, 2, 5-dimethylphenol, and 3, 5-dimethylphenol. We did not explore the higher phenols. Most of the residual neutral oil consisted of various ketones. Repeated careful fractionation resulted in the isolation and identification of methyl ethyl ketone, diethyl ketone, methyl isobutyl ketone, mesityl oxide, and phorone.

The ketones are probably intermediates in the formation of the phenols. There are three possible ways in which phenols can be formed from mixtures of alcohols and ketones: 1) closing long carbon chains; 2) via the formation of isophorone; and 3) via the condensation of the ketones with β-diketones or β-keto-aldehydes. In this case, it seemed to us that the last of these was most likely, and this was confirmed by our results. The condensate contained no alcohols besides the initial methanol. Isophorone can hardly be an intermediate compound, inasmuch as only 3, 5-dimethylphenol was secured when the phenols were produced via isophorone by the Ipatyev method [5], whereas we secured a complex mixture of phenols. These latter were produced only from a methanol-acetone mixture, neither methanol nor acetone giving rise to any phenols by itself, as was proved by special tests. The possibility of producing phenols by condensing ketones with diketones was also demonstrated experimentally. In our effort to establish the possible mechanism of the condensation of methanol and acetone, resulting in the formation of various phenols, we likewise condensed methanol with diacetone alcohols, mesityl oxide, and phorone, i.e., with the condensation products of acetone itself. In every instance the phenol yield was extremely low, never exceeding 2-3%, thus proving that these compounds could not be intermediates in the production of the phenols from methanol and acetone. The low yield of phenols secured in these condensations may be attributed to the partial reversible decomposition of the products into acetone, which is then converted with the methanol into phenols. We assumed that under our experimental conditions the phenols are formed via the intermediate formation of β-diketones or β-keto-aldehydes, which are themselves unstable thermally, so that they are not found in the end products. Schematically, the initial stages of the process should proceed as follows:

$$\begin{gathered}CH_3OH \rightarrow CH_2O + H_2O\\ CH_3COCH_3 + CH_2O \rightarrow CH_3-CO-CH_2-CH_2OH\\ CH_3-CO-CH_2-CH_2OH \rightarrow CO_3-CO-CH_2-CHO + H_2.\end{gathered}$$

There is no doubt about the first stage, since the condensates always contain formaldehyde. That a ketol was produced was not established directly, but when ethyl alcohol was condensed with acetone, we proved that a decomposition product of the ketol was present – we secured ethylideneacetone. Further condensation of the ketones with di- or aldoketones yields phenols, the general pattern of their formation being as follows:



R_1, R_2, R_3, and R_4 may be hydrogen atoms or aromatic radicals. As a result, we secure all the experimentally established phenols. The process involves the splitting out of water and the dehydrogenation of the intermediate products, as is evidenced by the results of the gas analyses, which indicate a high percentage of hydrogen (as much as 50%) in the reaction gas. We believe that our investigation may throw some light upon the mechanism involved in the formation of phenols during the destructive distillation of wood.

EXPERIMENTAL

The catalytic heterogenous condensation of methanol and acetone yielded a two-layer liquid condensate; the upper layer was a dark oil, while the lower layer was aqueous, consisting of the unreacted initial substances plus other products. The phenols were extracted from the oily layer by repeated extraction with 10% NaOH. The resultant phenolates were extracted with ether to free them of the neutral oils that had been partially entrained with the alkali. When the phenolates were decomposed with dilute H_2SO_4, the phenols separated out as oils or crystalline products. The latter were filtered out, and the filtrate was re-extracted with ether. After the ether solution had been dried and the ether driven off, we got a mixture of phenols, which was then fractionated. The neutral part of the condensate was processed similarly before being fractionated. The results of this preliminary treatment of the products are given in Table 1.

Analysis of the phenols. Of the numerous methods of analyzing the phenols described in the literature, we chose the method of identification given by Steinkopf and Hopner [2] and Holzman and Pilat [3], as the simplest and most convenient. In some instances, as stated above, we used the method of first separating the phenols given by Bruckner [4]. Analysis indicated that the crystalline product secured was 3,5-dimethylphenol. Recrystallization and sublimation yielded elongated acicular crystals with an m.p. of 66-68° (68° in the literature) and a b.p. of 219° (219.5° in the literature). Found: M 122, 123.4. $C_8H_{10}O$. Calculated: M 122.

TABLE 1

	Initial Mixture	Condensate		Lower layer		Phenols			Neutral oil
		Total	Upper layer / Lower layer	Driven off at 54-80°	Water	Total	Crystals	Oil	
Grams	2310	1675	955/720	1182	88	147.8	11.8	136	189
% of condensate	–	–	57/43	70.3	5.2	8.8	0.7	8.1	11.3
% of the initial mixture	–	72.5	41.2/31.3	51.3	3.8	6.4	0.5	5.9	8.2

We prepared the tribromide, which had an m.p. of 162-164° after three recrystallizations (the literature gives 163°).

Condensation with monochloroacetic acid and sodium hydroxide yielded an aryl glycolic acid with an m.p. of 85-86°, representing 3, 5-xylenoxyacetic acid.

Found %: C 66.32, 66.5; H 6.7, 6.9. $C_{10}H_{12}O_3$. Calculated %: C 66.66; H 6.7.

The phenolic oil was distilled with a dephlegmator, a product that boiled continuously from 175-233°. The high-boiling residue represented 30% by weight of the phenolic oil. It apparently contained extremely complicated phenols, which we did not analyze any further. The product, with a b.p. of 175-233°, was repeatedly fractionated, all the narrower fractions being collected (Table 2).

TABLE 2

Fraction No.	Temperature	(g)	(%)
1	178-182°	5.5	6.1
2	182-205	9.4	10.4
3	205-210	10.2	11.3
4	210-216	17.0	13.9
5	216-225	21.0	23.3
6	225-230	17.1	19.0
	Residue, losses	9.8	11.0

The first fraction was condensed with monochloroacetic acid and sodium hydroxide. As the solution was chilled, the slightly soluble sodium salt settled out. This yielded an arylglycolic acid, with an m.p. of 97-99°, which is the melting point of phenoxyacetic acid. Found %: C 63.0, 62.96; H 5.35, 5.56. $C_8H_8O_3$. Calculated %: C 63.13; H 5.3.

The filtrate contained the readily soluble sodium salt of m-cresoxyacetic acid, with an m.p. of 100-102° (the literature gives 103°).

Found %: C 64.88, 64.75; H 6.39, 6.27. $C_9H_{10}O_3$. Calculated %: C 65.03; H 6.07.

The second fraction was processed like the first one. The precipitated arylglycolic acids were dissolved in hot benzene, the crystals that settled out being filtered out (the operation being repeated several times) and then recrystallized four times from alcohol. The resultant product had an m.p. of 96-98°. Its mixed melting point confirmed the presence of phenoxyacetic acid. An acid with an m.p. of 84-86°, corresponding to 3, 5-dimethylphenoxyacetic acid, was recovered from the filtrate (the literature gives the m.p. as 86°).

The third fraction was also condensed with monochloroacetic acid and sodium hydroxide. The appropriate processing yielded a mixture of arylglycolic acids, which could not be separated by fractional crystallization. The fourth, fifth and sixth fractions were first separately processed as specified by Bruckner. The ether extracts of the aqueous distillates of all three of the initial fractions, collected at the same cleavage temperatures of the phenolsulfonic acids, were combined and dried. The phenols were isolated after the ether had been driven off. The results of our cleavage of the phenolsulfonic acids (50 g of phenol) are given in Table 3.

In every instance, a product that congealed into a colorless oil passed over up to 107°. Processing it in the usual manner yielded an acid with an m.p. of 84-86°, corresponding to 3, 5-dimethylphenoxyacetic acid (the literature gives its m.p. as 86°). We were unable to isolate any individual products from the 107-115° fraction. The 115-119° fraction is the principal fraction, containing 23% by weight of sulfonated phenols. Processing it with twice its weight of monochloroacetic acid and sodium hydroxide yielded two acids: m-cresoxyacetic, benzene-soluble, with an m.p. of 102-103°, and 2, 5-dimethylphenoxyacetic, soluble in petroleum ether, with an m. p. of 116-118° (the literature gives its m.p. as 118°). Elementary analysis of the latter acid yielded the following results:

TABLE 3

Fraction No.	Cleavage temperature	Phenol yield, grams	% of the initial phenol
1	up to 107°	6.2	12.4
2	107 - 115	3.7	7.4
3	115 - 119	11.5	23
4	120 - 125	6.6	13.2
5	125 - 136	5.4	10.8
	Losses	16.6	32.2

Found %: C 66.08, 66.36; H 6.9, 6.8; $C_{10}H_{12}O_3$. Calculated %: C 66.6; H 6.7.

The 120 - 125° fraction was converted into arylglycolic acids, the mixture yielding 0.5 g of a substance with an m.p. of 114 - 116°, which probably was 2,5-dimethylphenoxyacetic acid, which had been found in the preceding fraction.

Only an approximate answer can be given to the problem of the quantitative content of the individual phenols. The yields of the arylglycolic acids averaged 70 - 75% of the theoretical. The yields of the phenols after the sulfonic acids had been cleaved were about 76% of the original. The unavoidable losses in the recrystallization of small quantities of substances totaled 15 - 20%. The figures listed in Table 4 are of significance only for a comparative estimate of the results secured.

TABLE 4 Total Content of Individual Phenols

No.	Individual phenols	% of phenols
1	Phenol	1.2
2	m-Cresol	3.4
3	2,5-Dimethylphenol	6.1
4	3,5-Dimethylphenol	8.8
5	Phenols with b.p. > 230°	40.0

Analysis of neutral products. This included an investigation of the lower, aqueous layer of the condensate, which boiled in the 54 - 80° range, and an investigation of the alkali-insoluble neutral oil. We managed to isolate 12 g of methyl ethyl ketone, with a b.p. of 78 - 80°, from the mixture of unreacted methanol and acetone by repeated fractionation.

TABLE 5

Ketone	Ketone constants			Semicarbazone melting point	Analysis of semicarbazones	
	Boiling point	d_4^{20}	n_D^{20}		% Calculated	% Experimental
Methyl ethyl ketone						
Our data	78 - 80°	0.8062	1.3827	134 - 136°	32.53	32.79; 32.91
Figures in the literature	80	0.805	1.3791	136		
Diethyl ketone [1]						
Our data	102	0.8151	1.3924	137 - 139	29.37	29.51
Figures in the literature	102	0.81425	1.3927	138 - 139		
Methyl isobutyl ketone						
Our data	117.5	0.8041	1.4070	130 - 132	27.75	26.4; 26.21
Figures in the literature	116.8	0.8008	1.3959	134		
Mesityl oxide						
Our data	128 - 130	0.8690	1.4428	164 (with decomposition)	27.10	27.24; 27.48
Figures in the literature	130	0.8650	1.4439	164		
Phorone [2]						
Our data	M.p. 25.5 - 26.5	—	—	—	—	—

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[1] 2,4-Dinitrophenylhydrazone — m.p. 152 - 153° (the literature gives 156°).

[2] Found %: C 78.01, 78.38; H 10.26, 10.41. $C_9H_{14}O$. Calculated %: C 78.26; H 10.15.

Analysis of the oily product indicated that 43.5% of it had a b.p. in excess of 200°, constituting a complicated mixture of saturated and unsaturated carbonyl compounds. The product collected up to 220° (96 g) was rectified into a Todd-type column [6], with an efficiency of 25 theoretical trays. Carbonyl groups were qualitatively identified in all the collected fractions. We isolated the following individual ketones: 1) diethyl ketone, 2) methyl isobutyl ketone, 3) mesityl oxide, and 4) phorone. The characteristics of the substances recovered are listed in Table 5.

Analysis of gaseous products. At optimum conditions for the phenol yield the gases had the following composition: 42% H_2, 10.5% CO_2, 3.5% CO, 5% C_nH_{2n} hydrocarbons, 33% C_nH_{2n+2} hydrocarbons, 6% residue.

SUMMARY

1. A mixture of methanol and acetone passed over Al_2O_3 + 10% Fe_2O_3 at 400° yields a two-layer condensate containing 8.8% of phenols. Alumina containing no iron – like the individual methanol or acetone – produces no phenols. The variation of the phenol yield with the per cent of iron in the catalyst has been determined.

2. The phenolic portion of the condensate has been found to contain phenol, m-cresol, and 2,5- and 3,5-dimethylphenols.

3. The nonphenolic part of the condensate contains methyl ethyl ketone, diethyl ketone, methyl isobutyl ketone, mesityl oxide, and phorone.

4. The most probable mechanism for the formation of phenols, via β-diketones or β-keto-aldehydes, is proposed.

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Received July 21, 1950

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CATALYTIC CONDENSATION OF ALCOHOLS WITH KETONES

II. CONDENSATION OF METHANOL WITH METHYL ETHYL KETONE, ETHYL ALCOHOL WITH ACETONE, AND ACETONE WITH ACETYLACETONE

B. N. Dolgov and I. N. Samsonova

In our preceding report we described the process we have discovered for producing phenols by condensing methanol with acetone at 410° over an alumina catalyst containing iron. On the assumption that this was a general reaction, we undertook further research with the objective of demonstrating the applicability of these processes to other systems, and of confirming the correctness of the schema proposed by us for the formation of the phenols via β-diketones or β-keto-aldehydes in other instances. As will be seen below, our assumptions have been largely confirmed. Condensation of methanol with methyl ethyl ketone has yielded o-cresol mixed together with higher phenols, which were not investigated any further.

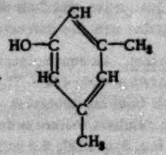
Condensing ethyl alcohol with acetone yielded 3,5-dimethylphenol as the sole phenol product, probably as follows:

$$C_2H_5OH \rightarrow CH_3CHO + H_2$$

$$CH_3COCH_3 + CH_3CHO \rightarrow CH_3COCH_2CHOHCH_3$$

$$CH_3COCH_2CHOHCH_3 \rightarrow CH_3COCH_2COCH_3 + H_2$$

$$CH_3COCH_2COCH_3 + CH_3COCH_3 \rightarrow 2H_2O +$$



The correctness of this schema is likewise borne out by the fact that the resultant condensate contained some ethylidene ketone, a product of the thermal decomposition of the β-ketol [1]

$$CH_3COCH_2CHOHCH_3 \rightarrow CH_3COCH{=}CHOH + H_2O.$$

When ethyl alcohol was condensed with acetone, no higher ketones were found in the nonphenolic part of the condensate, which is why no other phenols could be formed, according to the proposed schema.

When acetone was condensed with acetylacetone in order to check this schema, we secured the expected 2,5-dimethylphenol. All the results described below were secured under the optimum conditions (400-410°), with 8 ml of the initial mixture passing over the Al_2O_3 + 10% Fe_2O_3 catalyst per hour.

EXPERIMENTAL

1. Methanol-methyl ethyl ketone system. The two-layer condensate collected in numerous runs made under identical conditions was processed to separate the phenolic portion (cf Report I). The dried phenols (44 g) were rectified in a column with an efficiency of 25 theoretical trays, the following fractions being collection:

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[1] Claisen produced a β-ketol from acetone and acetaldehyde [1].

No.	Boiling point	Grams	Per cent
1	189 - 190°	2.5	5.7
2	205 - 216	0.4	0.9
3	216 - 218	2.5	5.7
4	218 - 225	4	9.1
	Above 225°	28.6	65.0
	Losses	6.0	13.6

All these fractions were analyzed for individual phenols by preparing the arylglycolic acids [2]. When the first fraction was condensed with monochloracetic acid and sodium hydroxide, we secured an arylglycolic acid with an m.p. of 150 - 152°, representing orthocresoxyacetic acid (this m.p. is given as 151 - 152° in the literature).

Found %: C 64.92; H 6.31. $C_9H_{10}O_3$. Calculated %: C 65.03; H 6.07.

When fractions 3 and 4 were allowed to stand in a freezing mixture, colorless crystals settled out, their m.p. being 80 - 81° after several recrystallizations.

Found %: C 79.27, 79.01; H 9.08, 8.99; M 131.1, 133.5. $C_9H_{12}O$. Calculated %: C 79.41; H 8.87; M 136.

These values are very close to the theoretical C and H content of methylethyl -or propylphenols. All our attempts to secure a crystalline arylglycolic acid from Fractions 3 and 4 met with failure, however. The residue, boiling over 225°, constituted 65% by weight of the total phenols. Nor were we able to secure crystalline arylglycolic acids from this residue. The percentage of hydroxyl groups in this residue was determined quantitatively. This was done by methylating part of the residue by the Heuser method [3], after which the methoxyl number was determined by the Viebock and Schupach method [4]. The hydroxyl percentage was found to be 12.6%. This indicated that the bulk of the phenols produced when methanol was condensed with methyl ethyl ketone consisted of high-boiling complicated phenols.

The neutral portion of the oil (80 g) was separated from the phenols and fractionated into a column. This yielded a series of fractions, each of which boiled in a wide temperature range. Analysis showed that none of them was an individual substance. Qualitative reactions indicated that the neutral oil was a complicated mixture of saturated carbonyl compounds together with the unreacted initial substances.

2. Ethyl alcohol - acetone system. An equimolecular mixture of rectified alcohol (94% ethyl alcohol) and acetone was passed over the catalyst at 400 - 410°. The resulting two - layer condensate was treated with an alkali solution to separate the phenols from the neutral reaction products. The phenols recovered by acidulating the alkaline solution were dried with calcined sodium sulfate and then distilled. Distillation of 25 g of phenols yielded the following fractions: 1) b.p. 215 - 218°, 6.5 g (27%); 2) 218 - 220°, 12 g (50 %); and 5.5 g (23%) residue and losses. The bulk of the phenols in this system boiled within the 215 - 220° range. Both of the fractions crystallized completely when allowed to stand in a freezing mixture. After the snow - white crystals had been recrystallized from alcohol, they had an m.p. of 66 - 68°. This yielded 12.8 g of the pure product, which proved to be 3, 5 - dimethylphenol upon analysis.

Found: M 121.8, 122.8. $C_8H_{10}O$. Calculated M 122.

Three grams of the crystals were condensed with 3 g of monochloroacetic acid and 3 g of sodium hydroxide. After the resultant arylglycolic acid had been recrystallized, it had an m.p. of 84 - 85° (the m.p. of 3, 5 - dimethylphenoxyacetic acid is 86°). Thus 3, 5 - dimethylphenol is the only phenol produced by condensing ethyl alcohol with acetone.

The lower, aqueous layer boiled in the 63 - 80° range and contained an unreacted mixture of ethyl alcohol and acetone. The neutral dephenolized portion of the oil distilled at 100 - 224° when rectified. Nine different fractions were collected, containing carbonyl compounds — ketones — plus aldehydes or keto - aldehydes in some instances. Redistillation of the 123 - 126° fraction yielded 4.2 g of ethylideneacetone:

B.p. 122-124°, d_4^{20} 0.8590, n_D^{20} 1.4373. Literature data: b.p. 124°, d_4^{20} 0.8560, n_D^{20} 1.4350.

A semicarbazide-semicarbazone of ethylideneacetone, with an m.p. of 124-126°, was prepared.

Found %: N 38.52, 39.01. $C_7H_{16}O_2N_6$. Calculated %: N 38.88.

Repeated fractionation of the 126-130° fraction yielded a substance with a b.p. of 127-128.5°, representing pure mesityl oxide (n_D^{20} 1.4442). The semicarbazone had an m.p. of 162-163°.

Found %: N 27.22; $C_7H_{13}N_3O$. Calculated %: N 27.10.

3. Acetone-acetylacetone system. An equimolecular mixture of the two reagents was passed over the catalyst at 400° at a rate of 8 ml per hour. The condensate was treated with alkali to recover the phenols as described above. The oily phenols thus recovered crystallized completely after distillation. Recrystallization from petroleum ether yielded snow-white crystals with an m.p. of 66-67°, which was that of the expected 3,5-dimethylphenol, m.p. 68°.

Found %: M 121.3, 123.1. $C_8H_{10}O$. Calculated: M 122.

Condensation with monochloroacetic acid and sodium hydroxide yielded an arylglycolic acid, the m.p. of which was 84-85.5° after two recrystallizations from alcohol (the literature gives this m.p. as 86°). Its mixed melting point with known-3,5-triphenoxyacetic acid exhibited no depression. As we expected, the principal product of the condensation of acetone with acetylacetone was 3,5-dimethylphenol.

SUMMARY

1. Condensing methanol with methyl ethyl ketone at 400° over Al_2O_3 containing added Fe_2O_3 yields some o-cresol plus a complicated mixture of higher phenols.

2. Condensing the ethyl alcohol-acetone system under the same conditions yields 3,5-dimethylphenol as the sole phenolic product.

3: Condensing acetone with acetylacetone, in order to check the hypothesis advanced to explain the formation of the phenols, yields the expected 3,5-dimethylphenol.

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Received July 21, 1950

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THE REACTIONS OF ORGANOMERCURY COMPOUNDS WITH AMIDES OF FATTY ACIDS

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In our preceding paper [1] we described a reaction in which radicals were split off from complete organomercury compounds by heating them with succinimide. We found that the reaction occurs very readily, one radical being split off and the corresponding succinimidic mercury derivative being formed. We were interested in determining whether other acid amides would react like succinimide. We did this by running tests with acetamide and diacetamide. When diphenylmercury was heated to 141 - 145° with acetamide, we secured a nearly quantitative yield of phenylmercuryacetamide, benzene being evolved:

$$(C_6H_5)_2Hg + CH_3CONH_2 \rightarrow C_6H_6 + C_6H_5HgHNCOCH_3.$$

Ditolylmercury and di-α-naphthylmercury reacted similarly, but with much more difficulty. When diethylmercury was heated for a long time with acetamide, no ethane was split off nor was an acetamide derivative formed. Raising the experimental temperature above 150° caused thermal decomposition of the diethylmercury to set in without the latter reacting with the acetamide.

Diphenylmercury reacted in about the same conditions with diacetamide:

$$(C_6H_5)_2Hg + (CH_3CO)_2NH \rightarrow C_6H_6 + C_6H_5HgN(COCH_3)_2.$$

Like the acetamide, diacetamide did not react with diethylmercury.

The acetamide and diacetamide derivatives of an arylmercury compound and hydrochloric acid produce quantitative yields of the arylmercury chloride. Phenylmercury iodide was synthesized by reacting sodium iodide with phenylmercuryacetamide and phenylmercurydiacetamide.

The acetamide derivatives of p-tolylmercury and α-naphthylmercury yielded the respective symmetrical derivatives of a diarylmercury when reacted with sodium iodide in the same fashion.

EXPERIMENTAL

I Reactions of complete organomercury compounds with acetamide. The organomercury compounds were reacted with acetamide in reaction vessels heated on an oil bath. The constituents were reacted together in the molten state. The reactions lasted from 4 to 12 hours. No by-products or tarring was observed during the reactions. The experimental findings are listed in Table 1.

TABLE 1

Test No.	R_2Hg	Grams of R_2Hg used for the reaction	Grams of CH_3CONH_2 used for the reaction	Oil bath Temperature	RH yield		$RHgHNCOCH_3$ yield	
					Grams	Per cent	Grams	Per cent
1	$(C_6H_5)_2Hg$	3.6	1.3	140 - 145°	0.6	75.0	3.1	92.8
2	$(p\text{-}CH_3C_6H_4)_2Hg$	1.9	0.6	200 - 210	0.5	100.0	0.6	35.4
3	$(\alpha\text{-}C_{10}H_7)_2Hg$ . .	2.9	6.0	140 - 145	0.6	74.1	0.6	25.0
4	$(C_2H_5)_2Hg$	4.9	2.2	140 - 150	–	–	–	–

Experiments 1 and 2 were performed in a round-bottomed flask with a sabre-shaped outlet tube, on which a small air-cooled condenser was mounted. During the reactions benzene (Test 1) and toluene (Test 2) condensed at the bend in the outlet tube. The benzene and toluene were identified by producing their nitro products. The benzene was nitrated to m-dinitrobenzene (m.p. 89°), and the toluene to 2,4-dinitrotoluene (m.p. 70°). Their mixed melting points with the pure substances exhibited no depression.

Experiment 3 was performed in a large test tube. The naphthalene produced in the reaction was driven off with steam. The melting point of the naphthalene secured was 80°, exhibiting no depression when mixed with the pure product.

The reaction of diethylmercury with acetamide (Test 4) was performed in a round-bottomed flask fitted with a reflux condenser and connected to a gas buret. No ethane was evolved when the temperature of the oil bath was about 140°, the initial reagents being recovered from the reaction mixture. Prolonged heating (up to 35 hours) at temperatures in excess of 150° resulted in the partial thermal decomposition of the diethylmercury into ethane, ethylene, and metallic mercury. No ethylmercuryacetamide was found in the reaction products.

In every case the organomercury derivatives were recovered from the reaction mixture by extracting them repeatedly with boiling water. After the extract had been evaporated and cooled with water, the organomercury derivative of acetamide settled out as a white amorphous powder. This was followed by double recrystallization from benzene. Pure products were secured, their physical properties being listed in Table 2.

TABLE 2

Test No.	$RHgHNCOCH_3$	Melting point (from benzene)	Solubility		
			Cold water	Hot water	Benzene
1	$C_6H_5HgHNCOCH_3$	167 - 168°	Sparing	Low	Good
2	$p\text{-}CH_3C_6H_4HgHNCOCH_3$	243 - 244	Sparing	Low	Good
3	$\alpha\text{-}C_{10}H_7HgHNCOCH_3$	199 - 203	Sparing	Low	Low

Phenylmercuryacetamide. 0.3604 g substance: 0.2604 g HgS. Found %: Hg 59.51. C_8H_9ONHg. Calculated %: Hg 59.77.

Tolylmercuryacetamide. 0.3124 g substance: 0.2070 g HgS. Found %: Hg 57.14. $C_9H_{11}ONHg$. Calculated %: Hg 57.38.

II. Reactions with HCl and NaI. The reactions were performed in a round-bottomed flask, fitted with a reflux condenser. Acetone was used as the solvent because of the low solubility of organomercury derivatives of acetamide in water. A sample of the test substance (0.05-0.2 g) was dissolved in boiling acetone, and then a solution of HCl (or NaI) in acetone was added. After boiling had proceeded for a short time, the excess solvent was driven off. The organomercury compound that settled out upon cooling was filtered out and dried. This was followed by recrystallization from benzene.

In every case the reaction products were identified by determining their melting points and their mixed melting points with the pure substances. The test results are listed in Table 3.

TABLE 3

No.	$RHgHNCOCH_3$	Reaction with HCl				
		Reaction product	Grams of initial substance used	Grams of product secured	% yield	Melting point
1	$C_6H_5HgHNCOCH_3$	C_6H_5HgCl	0.20	0.17	91.4	251°
2	$p\text{-}CH_3C_6H_4HgHNCOCH_3$	$p\text{-}CH_3C_6H_4HgCl$	0.25	0.23	98.7	233
3	$\alpha\text{-}C_{10}H_7HgHNCOCH_3$	$\alpha\text{-}C_{10}H_7HgCl$	0.15	0.12	85.7	189

No.	$RHgHNCOCH_3$	Reaction with NaI				
		Reaction product	Grams of initial substance used	Grams of product secured	% yield	Melting point
1	$C_6H_5HgHNCOCH_3$	C_6H_5HgI	0.06	0.06	90.2	271°
2	$p\text{-}CH_3C_6H_4HgHNCOCH_3$	$(p\text{-}CH_3C_6H_4)_2Hg$	0.10	0.05	92.5	238
3	$\alpha\text{-}C_{10}H_7HgHNCOCH_3$	$(\alpha\text{-}C_{10}H_7)_2Hg$	0.05	0.03	100	246

III. Reactions of diacetamide with diphenylmercury and diethylmercury. a) Reaction of diphenylmercury with diacetamide. The diacetamide was prepared by acetylating acetamide with acetic anhydride. 3.6 grams of diphenylmercury and 2.0 g of diacetamide were placed in a round-bottomed flask possessing a sabre-shaped outlet tube. The reaction flask was heated to 150-165° for 4 hours on an oil bath. Benzene condensed at the bend of the outlet tube. The benzene weighed 0.6 g, representing 75% of the theoretical. Nitration with benzene yielded 0.8 g of *m*-dinitrobenzene with an m.p. of 89°. Its mixed melting point exhibited no depression. The phenylmercurydiacetamide was extracted from the reaction mixture with hot water and recrystallized twice from the latter. This yielded 0.35 g of the pure substance with an m.p. of 152-153°. The yield of phenylmercurydiacetamide was 35.7%.

Phenylmercurydiacetamide is a white crystalline substance, freely soluble in hot water and the customary organic solvents.

0.2032 g substance: 0.1251 g HgS. Found %: Hg 53.10. $C_{10}H_{11}O_2NHg$. Calculated %: Hg 53.12.

b) Reaction of phenylmercurydiacetamide with HCl. 0.21 gram of phenylmercurydiacetamide was dissolved in hot water, and an alcoholic solution of concentrated hydrochloric acid was added. Phenylmercury chloride was precipitated instantaneously. The precipitate was filtered out, dried, and recrystallized from benzene. This yielded 0.17 g of the substance, representing 100% of the calculated yield. M.p. 251°, exhibiting no depression with pure phenylmercury chloride.

c) Reaction of phenylmercurydiacetamide with KI. A large excess of a hot solution of KI was added to a hot aqueous solution of 0.13 g of phenylmercurydiacetamide. An abundant white precipitate of phenylmercury iodide settled out. The precipitate was filtered out, dried, and twice recrystallized from benzene. This yielded 0.13 g of pure phenylmercury iodide (93.5%), with an m.p. of 266°. Its mixed melting point exhibited no depression.

d) Reaction of diethylmercury with diacetamide. 1.5 gram of diacetamide and 4.3 g of diethylmercury were placed in a reaction flask fitted with a reflux condenser and connected to a gas buret. The mixture was heated to 150-160° (oil bath) for 4.5 hours. After the reaction was over, the unreacted initial substances were recovered from the reaction vessel.

SUMMARY

1. The reactions of acetamide and diacetamide with organomercury compounds have been investigated.

2. Diarylmercury derivatives react by splitting off one radical as a hydrocarbon and forming an arylmercuryacetamide or an arylmercurydiacetamide.

3. Diethylmercury does not react when heated with acetamide or diacetamide.

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Received July 10, 1950

THE REACTIONS OF ORGANOMETALLIC COMPOUNDS WITH THIOSALICYLIC ACID AND THIOPHENOL

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The author has previously shown [1] that diphenylmercury yields benzene and the corresponding organomercury derivatives when reacted with various organic acids, in accordance with the general equation (1):

$$(C_6H_5)_2Hg + RCOOH \rightarrow C_6H_6 + RCOOHgC_6H_5 \qquad (1)$$

the hydroxy acids being the most reactive. The author later showed [2] that various organomercury compounds (Ar_2Hg, Alk_2Hg, ArHgOAc, etc.) readily mercurate phenol in accordance with Equation (2):

$$R_2Hg + R'C_6H_4OH \rightarrow RH + R'C_6H_3(OH)HgR. \qquad (2)$$

The reactions of organomercury compounds that contain an SH group with derivatives of the phenols and acids follow a totally different course. When diphenylmercury is reacted with the thiophenols [3], metallic mercury settles out, and benzene, disulfides, and mercury thiophenolates are produced (3):

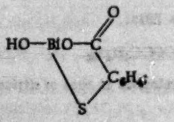
$$(C_6H_5)_2Hg + RC_6H_4SH \rightarrow Hg + C_6H_6 + (RC_6H_4S)_2Hg + (RC_6H_4S)_2. \qquad (3)$$

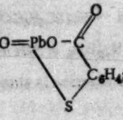
In the present paper we have made a study of the reaction of organometallic compounds with thiosalicylic and thioglycolic acids and have shown that mercury compounds of the RHgHal type, which do not react with the phenols at 150-175°, react readily with thiophenol at 130°. The following reactions were investigated: diphenylmercury with thioglycolic and thiosalicylic acids, RHgHal and R_2Hg with thiosalicylic acid, RHgHal with thiophenol, and $(C_6H_5)_3Bi$, $(C_6H_5)_4Pb$ and $(C_6H_5)_4Sn$ with thiosalicylic acid at 100-130°.

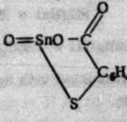
We know from the literature [4] that some RHgHal compounds react with thiosalicylic acid when an alcoholic alkali is present, yielding compounds of the $RHgSC_6H_4COOMe$ type, which possess strong antiseptic properties. When aromatic compounds of mercury, lead, tin and bismuth are reacted with thiosalicylic acid, hydrocarbons and the corresponding metallic derivatives of thiosalicylic acid are produced:

$$R_2Hg + 2HSC_6H_4COOH \rightarrow 2RH + Hg(SC_6H_4COOH)_2 \qquad (4)$$

The reaction takes place readily at 100-130°, 130° being required only in the case of tetraphenyllead. The stability of the metallic derivatives of thiosalicylic acid varies, mercuribisthiosalicylic acid, $Hg(SC_6H_4COOH)_2$, being the most stable compound. The lead, tin, and bismuth derivatives are readily hydrolyzed, yielding the basic salts:







In contrast to other organometallic compounds (Sn, Pb, and Bi), the aromatic compounds of mercury liberate metallic mercury when they are reacted with thiocarboxylic acids. The production of metallic mercury may be explained as an oxidation reaction of the thiosalicylic acid to diphenyldisulfodicarboxylic acid according to Equation (5):

$$R_2Hg + 2HSC_6H_4COOH \rightarrow Hg + 2RH + (HOOCC_6H_4S)_2. \qquad (5)$$

as well as the action of the mercuribisthiosalicylic acid, produced in Equation (4) with the solvent (alcohol), according to Equation (6):

$$Hg(SC_6H_4COOH)_2 + CH_3CH_2OH \rightarrow Hg + 2HSC_6H_4COOH + CH_3CHO. \qquad (6)$$

When diphenylmercury is reacted with thioglycolic acid, much less metallic mercury is thrown down (19%) than in the reaction with thiosalicylic acid (63%), and we are unable to isolate a stable mercury derivative of thioglycolic acid. Other aryl compounds of mercury react with thiosalicylic acid like diphenylmercury, with the sole exception of dibenzylmercury, which yields R – R (dibenzyl) instead of an RH hydrocarbon. The RHgHal organomercury compounds react readily with thiosalicylic acid and thiophenol at 100 - 130° (Tables 2 and 3).

TABLE 1

Reaction of R_2Hg with Thiosalicylic and Thioglycolic Acids

Test No.	R_2Hg	Thio acid	t°	Time, hours	% metallic Hg	Per cent $Hg(SC_6H_4COOH)_2$ produced	Other reaction products
1	Diphenylmercury	Thioglycolic acid	100°	6	1.95	–	–
2	Diphenylmercury	" "	130	3	6.60	–	–
3	"	" "	130	6	19.00	–	–
4	"	Thiosalicylic acid	100	3	15.8	24.0	Benzene
5	"	" "	100	6	33.6	40.0	"
6	"	" "	130	3	35.4	36.0	"
7	"	" "	130	6	43.5	41.0	"
8	"	" "	130	6	3.5	74.0	"
9	"	" "	130	6	21.0	56.0	"
10	"	" "	130	6	10.9	71.0	"
11	"	" "	130	6	63.7	20.0	"
12	Mercuribisthiosalicylic acid	" "	130	6	0.0	–	–
13	" "	" "	130	3	20.1	–	Thiosalicylic acid
14	" "	" "	130	6	30.2	–	" "
15	Ditolylmercury	Thiosalicylic acid	130	3	2.2	85.0	Toluene
16	Dibenzylmercury	" "	130	3	76.8	10.0	Dibenzyl
17	Dinaphthylmercury	" "	130	3	68.7	18.5	Naphthalene

NOTES: 1. The R_2Hg: thio acid ratio was 1:2 in all the tests, except in Test 10 (1:3 ratio) and Test 11 (1:10 ratio). 2. Alcohol was the solvent in all the tests, except: No. 8 (xylene) and No. 9 (no solvent used). 3. Reacting diphenylmercury with salicylic acid (1:2 ratio) for 3 hours at 130° yields phenylmercury salicylate, $C_6H_4(OH)COOHgC_6H_5$, quantitatively, no metallic mercury separating out.

When RHgHal is reacted with thiosalicylic acid, decomposition follows two lines, as in the case of R_2Hg, the sole difference being that Hg_2Hal_2 is formed instead of metallic mercury:

$$RHgHal + 2HSC_6H_4COOH \rightarrow Hg(SC_6H_4COOH)_2 + RH + HHal, \qquad (7)$$

$$2RHgHal + 4HSC_6H_4COOH \rightarrow Hg_2Hal_2 + 2RH + 2HHal + 2(HOOCC_6H_4S)_2. \qquad (8)$$

When RHgHal is reacted with thiophenol, the reaction is almost wholly analogous to that of diphenylmercury (Equation 3):

$$RHgHal + 2HSC_6H_5 \rightarrow Hg(SC_6H_5)_2 + RH + HHal, \qquad (9)$$

$$RHgHal + 2HSC_6H_5 \rightarrow Hg + RH + HHal + (C_6H_5S)_2. \qquad (10)$$

EXPERIMENTAL

All the experiments were performed by heating a mixture of the reagents in sealed ampoules immersed in thermostats whose temperatures were accurately controlled.

1. Diphenylmercury and thiosalicylic acid (130°, 3 hours). 0.5 gram of thiosalicylic acid was used with 0.5 g of diphenylmercury (1:2.2 ratio), plus 3 ml of alcohol. After the heating was over, benzene was found in the alcoholic solution, while 0.1004 g (35.44%) of metallic mercury was recovered from the precipitate, the

precipitate readily dissolving in a water-alcohol solution of alkali and settling out again when the solution was acidulated. Double reprecipitation and recrystallization from alcohol yielded 0.25 g of mercuribisthiosalicylic acid as white cubes with an m.p. of 250-251°. This compound was cleaved by prolonged boiling in an alcoholic solution of HCl, yielding $HgCl_2$ and thiosalicylic acid.

0.05 g substance: 1.97 ml 0.1 N NH_4CNS. Found %: Hg 39.42. $Hg(SC_6H_4COOH)_2$.
Calculated %: Hg 39.60.

The alcoholic mother liquor yielded 0.05 g of the light-yellow crystals of diphenyldisulfidedicarboxylic acid, with an m.p. of 286° (the m.p. is given in the literature as 288°).

TABLE 2
Reaction of RHgHal with Thiosalicylic Acid

No.	RHgHal	t°	Time, hours	Per cent Hg_2Hal_2	Per cent $Hg(SC_6H_4COOH)_2$ produced	Other reaction products
1	C_6H_5HgCl	130°	3	–	64.0	HCl, C_6H_6
2		130	6	18.0	46.3	HCl, C_6H_6
3	C_6H_5HgBr	100	6	–	16.0	HBr, C_6H_6
4		130	3	7.0	60.0	HBr, C_6H_6
5		130	6	21.2	53.5	HBr, C_6H_6
6	$CH_3C_6H_4HgBr$	100	6	–	30.0	HBr, $C_6H_5CH_3$
7		130	3	4.8	56.0	HBr, $C_6H_5CH_3$
8		130	6	33.3	50.0	HBr, $C_6H_5CH_3$
9	$C_{10}H_7HgBr$	130	3	14.2	58.0	HBr, $C_{10}H_8$
10	$C_6H_{11}HgBr$	130	3	1.5	40.0	–
11	C_2H_5HgBr	130	3	1.0	34.0	–

NOTES: 1. The following quantities were used in all the tests: 0.001 mole of RHgHal; 0.002 mole of thiosalicylic acid; and 3 ml of alcohol. 2. Mercuribisthiosalicylic acid, $Hg(SC_6H_4COOH)_2$, with an m.p. of 250-251° and a mercury content of 39.35-39.55% (theoretical content = 39.60%), was produced in every test. 3. No reaction occurred when C_6H_5HgBr and C_2H_5HgBr were reacted with salicylic acid at 130°.

TABLE 3
Reaction of RHgHal with Thiophenol

No.	RHgBr	t°	Time, hours	% metallic Hg	% $Hg(SC_6H_4COOH)_2$ produced
1	C_6H_5HgBr	130°	3	28.6	70
2	$CH_3C_6H_4HgBr$	130	3	9.3	86
3		130	6	32.9	65
4	C_2H_5HgBr	130	6	24.7	72

NOTES: 1. 0.3 gram of RHgBr, 0.3 g of thiophenol, and 3 ml of alcohol used in all tests. 2. Mercury thiophenolate, $Hg(SC_6H_5)_2$, with an m.p. of 150-151° and a mercury content of 47.60-47.75% (theoretical content = 47.92%), was produced in every test, and diphenyl disulfide (0.1-0.12 g) was formed. 3. No reaction occurred when C_2H_5HgBr or C_6H_5HgBr was heated to 150° with phenol, cresol, nitrophenols, and resorcinol.

2. Phenylmercury chloride and thiosalicylic acid (130°, 6 hours). 0.65 g of thiosalicylic acid was used for 1.0 g of phenylmercury chloride (1:1.3), plus 5 ml of alcohol. HCl and benzene were found in the alcoholic solution after it had been heated. Hg_2Cl_2 (18%) and 0.75 g of mercuribisthiosalicylic acid, with an m.p. of 250°, were recovered from the precipitate.

0.052 g substance: 2.05 ml 0.1 N NH_4CNS. Found %: Hg 39.42. $Hg(SC_6H_4COOH)_2$. Calculated %: Hg 39.60.

3. Phenylmercury bromide and thiosalicylic acid (130°, 6 hours). 0.65 g of thiosalicylic acid was used for 1.0 g of phenylmercury bromide (1:1.5 ratio), plus 5 ml of alcohol. HBr, benzene, and Hg_2Br_2 (21.2%) were found in the reaction products. 0.75 gram of mercuribisthiosalicylic acid, with an m.p. of 250-251°, was recovered.

0.055 g substance: 2.16 ml 0.1 N NH_4CNS. Found %: Hg 39.27. $Hg(SC_6H_4COOH)_2$. Calculated %: Hg 39.60.

4. p-Tolylmercury bromide and thiosalicylic acid (130°, 6 hours). 0.62 g of thiosalicylic acid was used for 1.0 g of tolylmercury bromide (1:1.5 ratio), plus 5 ml of alcohol. HBr, toluene, and Hg_2Br_2 (33.37%) were found in the reaction products. 0.68 g of mercuribisthiosalicylic acid, with an m.p. of 250-252°, was recovered.

0.0482 g substance: 1.89 ml 0.1 N NH_4CNS. Found %: Hg 39.21. $Hg(SC_6H_4COOH)_2$. Calculated %: Hg 39.60.

5. Mercuric bromide and thiosalicylic acid. Mercuric bromide and thiosalicylic acid (1:2 ratio), dissolved in alcohol, yielded HBr and mercuribisthiosalicylic acid, at room temperature as well as when heated to 130°.

0.0491 g substance: 1.94 ml 0.1 N NH_4CNS. Found %: Hg 39.51. $Hg(SC_6H_4COOH)_2$. Calculated %: Hg 39.60.

6. Triphenylbismuth and thiosalicylic acid (100°, 3 hours). 1.05 grams of thiosalicylic acid was used for 1.0 g of triphenylbismuth (1:3 ratio), plus 6 ml of alcohol. Benzene was found in the alcoholic solution. The precipitate yielded 0.63 g of lustrous yellow crystals, which did not melt below 300° and were insoluble in organic solvents. These crystals dissolved at once in mineral acids, losing their color and yielding thiosalicylic acid and the respective $Bi^{\cdots}$ salts.

0.1114 g substance: 0,0892 g $BiPO_4$. Found %: Bi 55.41. $C_7H_5O_3SBi$. Calculated %: Bi 55.29.

A similar derivative of thiosalicylic acid and bismuth was formed at 130°.

7. Tetraphenyllead and thiosalicylic acid (130°, 3 hours). 0.96 gram of thiosalicylic acid was used for 0.78 g of tetraphenyllead (1:4 ratio), plus 6 ml of alcohol. Benzene was found in the alcoholic solution after heating was over. Repeated processing of the precipitate with solvents yielded 0.57 g of lustrous white lamellae, which did not fuse up to 315°, were insoluble in organic solvents, were slightly soluble in alkali solutions and were readily soluble in mineral acids.

0.0690 g substance: 0.0560 g $PbSO_4$. Found %: Pb 55.36. $C_7H_4O_3SPb$. Calculated %: Pb 55.20

8. Tetraphenyltin and thiosalicylic acid (130°, 6 hours). 1.38 g of thiosalicylic acid was used for 0.96 g of tetraphenyltin (1:4 ratio), plus 8 ml of alcohol. Benzene was found in the alcoholic solution after heating was over. The precipitate yielded 0.5 g of a lemon-yellow powder, which did not fuse up to 320°, was insoluble in organic solvents and readily soluble in mineral acids

0.092 g substance: 0.0480 g SnO_2. Found %: Sn 41.10. $C_7H_4O_3SSn$. Calculated %: Sn 41,47.

SUMMARY

1. When the aromatic compounds of mercury, lead, tin, and bismuth are reacted with thiosalicylic acid, they yield hydrocarbons and metallic derivatives of the thiosalicylic acid of the $Me^x(SC_6H_4COOH)_x$ type.

2. When organomercury compounds of the RHgHal type are reacted with thiosalicylic acid, they yield $Hg(SC_6H_4COOH)_2$, RH, HHal, and Hg_2Hal_2.

3. When organomercury compounds of the RHgHal type are reacted with thiophenol, they yield $Hg(SC_6H_5)_2$, RH, Hg and $(C_6H_5S)_2$.

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Received June 17, 1950.

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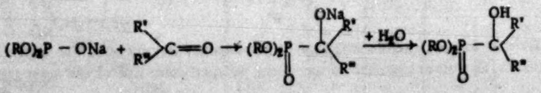
THE REACTION OF DIALKYLPHOSPHOROUS ACIDS WITH ALDEHYDES AND KETONES

A NEW METHOD OF SYNTHESIZING ESTERS OF ALPHA HYDROXYALKYLPHOSPHINIC ACIDS

V. S. Abramov

Not much research has been done on the alpha hydroxyalkylphosphinic acids and their derivatives. The obvious reason is the difficulty of synthesizing and isolating them. The alpha hydroxyalkylphosphinic acids were first synthesized by Fossek [1] by reacting phosphorous trichloride with aldehydes or ketones and then treating the reaction products with water. Fossek secured several acids in this manner, but he was unable to produce the simplest hydroxymethylphosphinic acid. Then Marie [2] produced several alpha hydroxyalkylphosphinic acids by heating aldehydes and ketones with phosphorous acid or by reacting them with hypophosphorous acid and oxidizing the reaction products with bromine or mercuric chloride. Page [3] modified Fossek's method somewhat and secured a high yield of hydroxymethylphosphinic acid by reacting paraformaldehyde with phosphorus trichloride. Subsequently, A. E. Arbuzov and Kushkova [4] secured alpha hydroxymethylphosphinic acid by saponifying the ethyl ester of hydroxymethylphosphinic acid. Conant, McDonald, and Kinney synthesized various α-hydroxyphosphinic acids by reacting aldehydes and ketones with phosphorus trichloride, using various reagent ratios and temperatures, and then decomposing the reaction products with acetic acid. Conant and his associates likewise investigated the mechanism of this reaction. Fossek [1] isolated the diethyl ester of alpha hydroxyisoamylphosphinic acid as an oil by treating the product of the reaction between phosphorus trichloride and isovaleraldehyde with alcohol. Marie [2] secured the dimethyl ester of alpha hydroxybenzylphosphinic acid from the acid's silver salt and methyl iodide. A. E. Arbuzov and Kushkova [4] secured the diethyl ester of alpha hydroxymethylphosphinic acid by reacting sodium diethylphosphite with the ethyl ester of iodomethylphosphinic acid in aqueous alcohol. Kabachnik and Rossiiskaya [6] secured the dimethyl and diethyl esters of alpha hydroxybenzylphosphinic acid by reducing esters of alpha ketophosphinic acids with sodium amalgam in aqueous-alcoholic acetic acid.

The present paper describes a new method of preparing the diesters of alpha hydroxyalkylphosphinic acids. The method involves the direct action of aldehydes and ketones upon salts of dialkylphosphorus acids, as follows:

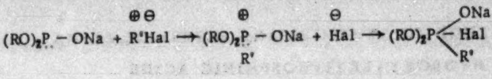


$$(RO)_2P-ONa + R'R''C{=}O \rightarrow (RO)_2P(=O)-C(ONa)R'R'' \xrightarrow{+H_2O} (RO)_2P(=O)-C(OH)R'R''$$

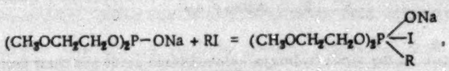
Diesters of alpha hydroxyalkylphosphinic acids were secured by treating the reaction products with acidulated water.

We are the first to have observed the addition of a sodium dialkylphosphite at the double bond in the carbonyl group of aldehydes and ketones. A. E. Arbuzov and Azanovskaya [7] had previously suggested a schema for the addition of sodium diethylphosphite at the carbonyl group of an ester of an alpha ketophosphinic acid by way of explaining the mechanism of the reaction of acetyl chloride with sodium diethylphosphite. They showed that an ester of alpha ketophosphinic acid reacts with sodium diethylphosphite. They did not isolate the reaction product, but they treated it with acetyl chloride. This resulted in the same product as that secured when acetyl chloride was reacted with sodium diethylphosphite, which, they thought, confirmed the schema they had advanced. They did not establish the structure of the end product, relying solely upon their determination of its molecular weight.

Esters of alkylphosphinic acids can be prepared in various ways [8]. The oldest and most commonly used is the method of Michaelis and Becker [9], involving the action of halides upon salts of dialkylphosphorous acids. We believe that this reaction may be regarded as the addition of a cationoid carbon atom of the alkyl halide to the phosphorus atom carrying a single electron pair, as follows:

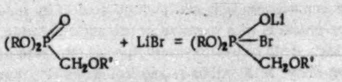


We have shown [10] that the action of iodides upon sodium di-β-methoxyethylphosphite in the customary Michaelis-Becker reaction results in the formation of addition products in accordance with the following equation:



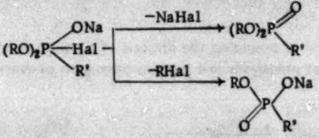
which is proof of the correctness of the schema set forth above.

Similar products are secured when lithium halides (LiBr, LiI) are reacted with esters of an alkoxymethylphosphinic acid, as follows:



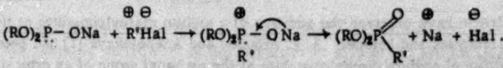
The lithium halide is added at the P═O bond when heat is applied. The addition products are recovered in the pure state.

Since alkylphosphinic acids and sodium halides are usually produced in the Michaelis-Becker reaction, the foregoing addition products must be intermediate ones, which suffer ready and rapid decomposition. Far from all reactions of this type produce high yields of alkylphosphinic acids. This may be due to the stability of the intermediate addition product and its subsequent decomposition in another manner. Heating the foregoing products of the addition of iodides to sodium di-β-methoxyethylphosphorous acid and of the addition of a lithium halide to esters of an alkoxymethylphosphinic acid yields a salt of an ester of an alkylphosphinic acid. Hence, decomposition follows two paths, as in the following equation:



Whether the sodium halide or the alkyl halide will be split out depends largely upon the nature of the radical attached to the phosphorus, as well as upon the nature of the halogen atom and of the ester groups and the experimental conditions.

The formation of esters of alkylphosphinic acids in the Michaelis reaction may be represented as follows:



It follows from the interpretation of the Michaelis-Becker reaction as the addition of a cationoid carbon atom to the phosphorous that not only halides, but other substances, whose molecules are polarized like the halides, can react with salts of dialkylphosphorous acids. It was only natural that this analogy be extended to the aldehydes and ketones, the molecules of which are also polar. The reaction with aldehydes or ketones is as follows:

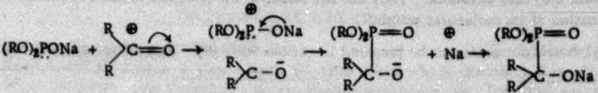
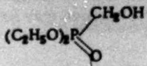
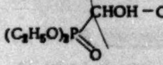
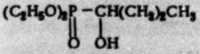
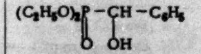
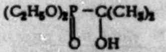
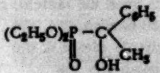
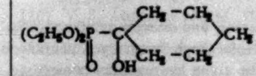
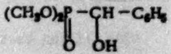
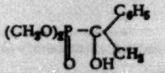
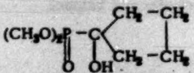
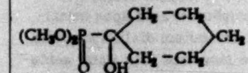
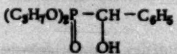
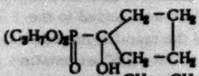
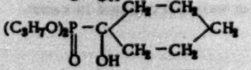
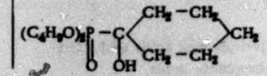


Table of the Diesters of Alpha Hydroxyalkylphosphinic Acids

No.	Formula of ester of alpha hydroxyalkylphosphinic acid	Boiling or melting point	d_4^{20}	n_D^{20}	MR_D		Phosphorus content	
					Experimental	Calculated	Experimental	Calculated
1		124 - 126° (3 mm)	1.1396	1.4322	38.1	37.2	18.07, 18.43	18.45
2		139 - 140 (6 mm)	1.119	1.4308	42.2	41.8	16.84, 16.89	17.03
3	 $(C_2H_5O)_2P(=O)-CH(OH)(CH_2)_2CH_3$	165 - 167 (18 mm)	1.071	1.4371	51.3	51.0	14.97, 14.68	14.76
4	 $(C_2H_5O)_2P(=O)-CH(OH)-C_6H_5$	82 - 83	–	–	–	–	– –	–
5	 $(C_2H_5O)_2P(=O)-C(OH)(CH_3)_2$	130 - 131 (10 mm)	1.0887	1.4318	46.7	46.4	15.84, 15.95	15.81
6		132 (3 mm)	1.122	1.4870	66.13	65.9	11.83, 11.95	12.01
7		72 - 73	–	–	–	–	12.96, 12.82	13.13
8	 $(CH_3O)_2P(=O)-CH(OH)-C_6H_5$	101 - 102	–	–	–	–	– –	–
9		134 - 135	–	–	–	–	13.29, 13.35	13.48
10		77 - 78	–	–	–	–	15.70, 15.84	15.98
11		118 - 119	–	–	–	–	14.52, 14.38	14.90
12 [1]	 $(C_3H_7O)_2P(=O)-CH(OH)-C_6H_5$	95 - 97	–	–	–	–	11.07, 11.21	11.35
13 [1]		63 - 63.5	–	–	–	–	12.16, 12.29	12.40
14 [1]		95 - 97	–	–	–	–	11.52, 11.61	11.74
15		46 - 47.5	–	–	–	–	10.42, 10.33	10.61

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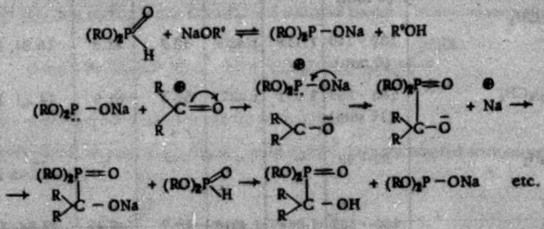
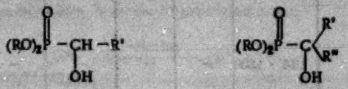
[1] C_3H_7 = isopropyl.

It must be supposed that aldehydes and ketones will also react with dialkylphosphorous acids if the acids have an enolic structure or are enolized during the reaction. B. A. Arbuzov and Pudovik [11] have shown that when sodium alcoholate is present, dialkylphosphorous acids add activated nitrile, carbonyl, and carboxyl groups at the ethylene bond. This method has been applied to reactions of aldehydes and ketones with dialkylphosphorous acids. The alcoholates of alkali metals, which enolize a dialkylphosphorous acid, make this reaction possible. In practice, a few drops of lithium or sodium methylate were used in our experiments. The reaction may be pictured as follows:



This chain reaction is rapid, considerable heat being evolved, and in most cases the yield of an ester of the alpha hydroxyalkylphosphinic acid is high. The completeness of the reaction depends upon the radicals in the carbonyl group: if the radicals reinforce the polarization of the molecule, the reaction is energetic, the yield being nearly quantitative, as in the case of benzoic aldehyde, whereas when the radicals diminish the polarization effect of the molecule, the reaction is moderated, and the yields are correspondingly low.

We have investigated the action of dimethylphosphorous, diethylphosphorous, and diisopropylphosphorous acids upon formaldehyde, acetaldehyde, butyraldehyde, benzaldehyde, acetone, acetophenone, cyclopentanone, and cyclohexanone. This resulted in production of the respective diesters of the alpha hydroxyalkylphosphinic acids, whose composition is:



R = CH_3, C_2H_5, and iso-C_3H_7; R' and R" are the radicals of the respective aldehydes and ketones.

EXPERIMENTAL

Action of aldehydes and ketones upon sodium dialkylphosphite. The sodium dialkylphosphite was prepared by the A. E. Arbuzov method [12], involving the action of a dialkylphosphorous acid upon metallic sodium in anhydrous ether. An aldehyde or a ketone was added to the resultant sodium dialkylphosphite, the reaction mass heating up until the ether boiled. The reaction products were processed with water acidulated with hydrochloric acid. The ether layer was separated and dried. After the ether had been driven off, the residue either crystallized or was distilled in vacuo.

Action of aldehydes and ketones on dialkylphosphorous acids. Equimolecular quantities of the aldehyde or ketone and the dialkylphosphorous acid. Some drops of lithium or sodium methylate were added to the mixture. The progress of the reaction was checked by the rise in the temperature of the reaction mixture as the alcoholate was added. The temperature rose 30 to 60°, as a rule; then heating to 100-125° was continued for a short time. The reaction products either crystallized upon cooling or were fractionated in vacuo.

The experimental findings are listed in the table.

SUMMARY

1. A new reaction has been found for the interaction of salts of dialkylphosphorous acids with aldehydes and ketones, resulting in the formation of esters of alpha hydroxyalkylphosphinic acids.

2. This reaction with dialkylphosphorous acids is easier and simpler when alcoholates are present.

3. This reaction holds both for aldehydes and ketones.

4. The new reaction makes it possible to synthesize a large number of various esters of alpha hydroxyalkylphosphinic acids.

5. The synthesized esters can be employed as the initial substances for further investigations.

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Received July 14, 1950

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1) See Consultants Bureau English translation, p. 315.

USING KETENE AS AN ACETYLATING AGENT

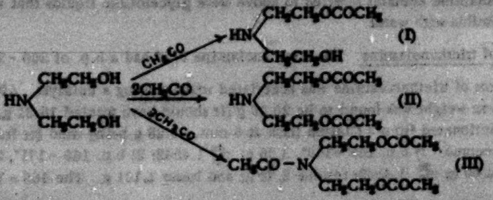
III. ACETATES OF DI- AND TRIETHANOLAMINES

A. A. Ponomarev and Yu. B. Isaev

The ethanolamines and their numerous derivatives are widely employed in various industries. In the past, however, the acetates of the ethanolamines have been known only as their derivatives [1, 2, 3], except for triethanolamine triacetate, which was synthesized by Ciusa and Sollazo, who used acetic anhydride and phosphoric acid [4].

We have reported [5] that high yields of the monoacetate and the diacetate are secured, depending on the conditions employed, when monoethanolamine is reacted with ketene. Sodium acetate is the most effective catalyst in synthesizing monoethanolamino diacetate. The N-monoacetate is produced by reacting an aqueous solution of monoethanolamine with ketene; this method is based upon the difference in the reaction rates of ketene with the primary amino group and the hydroxyl group. The present paper sets forth the results of our experiments on the acetylation of di- and triethanolamines with ketene.

The acetylation of diethanolamine is rather complicated, due to the presence of chemically different reactive groups in that compound. The formation of the reaction products (I), (II), and (III) may be predicted:



In our experiments on the acetylation of diethanolamine with ketene we secured mixtures of acetates; we were unable to effect complete separation of the constituents of these mixtures by means of distillation.

Under the same conditions triethanolamine gave us 90 - 93% yields of the triacetate. This is apparently due to the fact that equivalent functional groups participated in the acetylation reaction in this instance, i.e., there is no fundamental difference between this process and the acetylation of such polyfunctional compounds as the glycols. It may be that the high yield of the triacetate (90%) when triethanolamine is acetylated without a catalyst is related to the catalytic action of the triethanolamine upon the products of its own acetylation.

EXPERIMENTAL[1]

The ketene used in acetylation was produced in apparatus of our own design [6]. Acetylation was effected in small round-bottomed flasks fitted with outlet tubes, the ketene being bubbled (together with its accompanying gases) through a sample of the substance under acetylation. The reactors were immersed in water at 56 - 58° during acetylation.

Acetylation of diethanolamine. The diethanolamine had a b.p. of 141 - 144° (5 mm). 1. 20.00 grams of diethanolamine was acetylated without using a catalyst. The gain in weight was 17.91 g (the added weight should have been 16.20 g, based on the synthesis of a diacetyl derivative). The 37.26 g of reaction products was fractionated at 10 mm from a flask fitted with a herringbone dephlegmator.

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[1] S. G. Tsypkina assisted in the experimental work (analyses).

In our determinations of the MR_D and the elementary composition of the fractions, we always secured values that lay between those theoretically computed for the di- and triacetates, which was evidence that a mixture of these products that was hard to separate had been produced. The diacetyl derivative may predominate in the reaction products. The same results were secured when the experiment was repeated.

2. 15.06 grams of diethanolamine was acetylated with sodium acetate present. The gain in weight after the acetone had been driven off was found to be 16.80 g (the gain in weight should have been 12.04 g, basedon the production of a diacetyl derivative). The 39.08 g of reaction products was vacuum-distilled at 9 mm from a flask fitted with a herringbone dephlegmator. A 165 - 183° fraction was collected (14.23 g). Distillation was continued at 15 mm, yielding a fraction with a b.p. of 179 - 183° (12.79 g; n_D^{20} 1.4602; d_4^{20} 1.1468). Refractionation at 5 mm of the 165 - 183° fraction yielded the following fractions: 1.70 g, b.p. up to 173°; 3.14 g, b.p. 173 - 179°; and 6.99 g, b.p. 179 - 182°, which were investigated together with the 179 - 183° (15 mm) fraction mentioned above.

Comparison of the MR_D values and of the elementary analysis findings indicates that acetylation of diethanolamine with ketene in the presence of sodium acetate resulted in a difficultly separable mixture of acetyl derivatives of diethanolamine with the triacetyl derivative predominating.

3. 15.36 grams of diethanolamine was acetylated with $KHSO_4$ present [7]. The gain in weight totalled 11.28 g (it should have been 12.28 g, based on the diacetate). The 25.37 g of product was fractionated from a Claisen flask at 5 mm. The 181 - 183° fraction (8.62 g; n_D^{20} 1.4654; d_4^{20} 1.1527), and the 183 - 184° fraction (4.74 g; n_D^{20} 1.4780; d_4^{20} 1.1578), were investigated.

Comparison of the MR_D values and of the elementary analysis findings indicates that when $KHSO_4$ is present, we get a mixture of acetyl derivatives of diethanolamine, with the diacetate predominating. The mixtures of diethanolamine acetates referred to above were glycerollike liquids that were soluble in benzene and alcohol and miscible with water.

Acetylation of triethanolamine. The triethanolamine used had a b.p. of 200 - 202° (9 mm).

1. 19.28 grams of triethanolamine was acetylated without using a catalyst. After the acetone had been driven off, the gain in weight was found to be 20.00 g (it should have totaled 16.31 g, based on the triacetate). The product was fractionated from a Claisen flask at 5 mm, 39.28 g being used for fractionation. The following fractions were secured: 1) b.p. 165 - 169°, 3.56 g; n_D^{20} 1.4542; 2) b.p. 169 - 171°, 29.43 g; n_D^{20} 1.4494; 3) b.p. 171 - 172°, 2.50 g; n_D^{20} 1.4502; residue 2.78 g; and losses 1.101 g. The 169 - 171° fraction was analyzed.

0.1232 g substance: 0.2374 g CO_2; 0.0816 g H_2O. 0.2334 g substance: 10.5 ml N_2 (21.5°, 756.5 mm) Found %: C 52.58; H 7.40; N 5.10. $C_{12}H_{21}O_6N$. Calculated %: C 52.35; H 7.69; N 5.09.

The analysis data indicate that the experiment produced about 90% of the theoretical yield of triethanolamine triacetate.

2. 20.03g of triethanolamine was acetylated with 0.5 g of sodium acetate present until the gain in weight totaled 22.73 g (after the acetone had been driven off). The gain in weight should have been 16.93 g, based on the triacetate. The 42.76 g of product was fractionated from a Claisen flask at 7.8 mm, fractions with an aggregate weight of 34.64 g being collected in the 179-179.5° range. The residue (a solid) weighed 6.59 g; the losses totaled 0.97 g. The constants of the principal fraction were:

$$d_4^{20}\ 1.1130;\quad n_D^{20}\ 1.4488;\quad MR_D\ 66.32;\quad \text{calculated } 66.52.$$

0.2410 g substance: 11.0 ml N_2 (20.3°, 755.3 mm). 0.2562 g substance: 11.9 ml N_2 (20.1°, 752.4 mm). Found %: N 5.19, 5.26. $C_{12}H_{21}O_6N$. Calculated %: N 5.09.

The yield of triethanolamine was 93.8% of the theoretical in Experiment 2. Triethanolamine triacetate is a glycerollike, odorless, yellowish liquid. Its relative viscosity was 12.685 (against water at 20.20°). Triethanolamine triacetate is sparingly soluble in water, and soluble in alcohol, ether, and benzene.

SUMMARY

1. Diethanolamine has been acetylated with ketene under various conditions. It has been found that this yields a mixture of products at various stages of acetylation, which are hard to separate.

2. Triethanolamine has been acetylated with ketene, with and without sodium acetate present as a catalyst. The respective yields of triethanolamine triacetate are 93.80% and 90% of the theoretical.

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Received June 27, 1950

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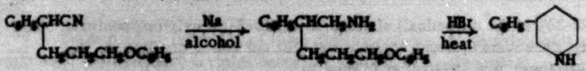
SYNTHESES EMPLOYING ACRYLONITRILE

XV. SYNTHESIS OF 3-PHENYL- AND 3,4-DIPHENYLPIPERIDINE

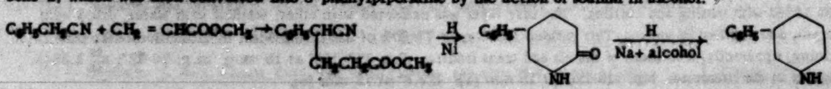
A.N.Kost and A.P.Terentyev

The β-arylpiperidines are cyclic analogs of the physiologically active bases of the phenamine type. That is why the physiological activity of 3-phenyl- [1] and 3,4-diphenylpiperidines [2] has been the subject of research, but the methods available for synthesizing these compounds were so complicated that it has been practically impossible to engage in any widespread product testing.

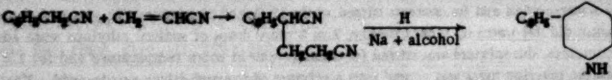
The synthesis of 3-phenylpiperidine by reducing the nitrile of α-phenyl-ω-phenoxyvaleric acid and then cyclizing it has been described [1]:



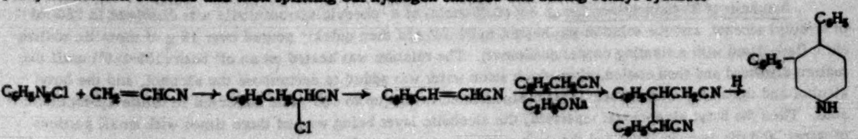
Koelsch [3] reacted methyl acrylate with benzyl cyanide and reduced the resultant methyl ester of γ-cyano-γ-phenylbutyric acid with skeletonized nickel (in alcohol at 200 atm and 150°), securing 5-phenylpiperidone-2, which was then converted into 3-phenylpiperidine by the action of sodium in alcohol.



We reacted benzyl cyanide with acrylonitrile and reduced the resultant α-phenylglutarodinitrile by the Vyshnegradsky method [4], i.e., with sodium in alcohol, immediately securing 59% of the theoretical yield of 3-phenylpiperidine.



Similarly, we secured yields up to 45% of the theoretical of 3,4-diphenylpiperidine by reducing the dinitrile of α,β-diphenylglutaric acid. We prepared the initial α,β-diphenylglutarodinitrile by reacting acrylonitrile with phenyldiazonium chloride and then splitting out hydrogen chloride and adding benzyl cyanide:



EXPERIMENTAL

Synthesizing α-phenylglutarodinitrile. 29.3 g (0.25 mole) of freshly distilled benzyl cyanide (b.p. 106-107° at 10 mm) and 13.7 g (0.3 mole) of acrylonitrile were placed in a 100-ml round-bottomed flask fitted with a reflux condenser. Then the mixture was shaken as 3 ml of sodium ethylate solution (1 g of sodium in 10 ml of absolute ethyl alcohol) was added. The mixture heated up spontaneously, the temperature rise being moderated by external water-cooling. After 20-30 minutes had elapsed, the violent reaction subsided, and the flask was heated for 30 minutes on a water bath (50-55°); after it had cooled, another 2 drops of sodium ethylate was added. The mixture was kept at room temperature for 4 hours, and then the flask's contents (a dark-olive liquid) were poured into 100 ml of 5% acetic acid. The organic layer was separated, washed with 10 ml of water, and dried with potash, the unreacted acrylonitrile being driven off, and the residue distilled in vacuo. This yielded 19.3-19.6 g (i.e., 45-46% of the theoretical) of α-phenylglutarodinitrile, with a b.p. of 184-187° at 9 mm. Refractionation yielded a b.p. of 181-183° at 8.5 mm; n_D^{25} 1.5237; d_4^{25} 1.0561; MR_D 49.31. $C_{11}H_{10}N_2$. Calculated 48.90.

Koelsch gives the b.p. at 198-200° at 18 mm. The yields when sodium methylate was used as a catalyst at 30-35° were: 36% in ether; 25% in an excess of phenylacetonitrile, and 0% in methanol or ethyl alcohol [5].

Synthesis of cinnamonitrile. 30 g of acetic acid and 100 ml of water were placed in a one-liter flask fitted with a mechanical stirrer, a thermometer, a reflux condenser, and a dropping funnel, and 70 ml of 40% potassium hydroxide was added. Then 15 g of cupric chloride, 250 ml of acetone, and 25 g (0.475 mole) of freshly distilled acrylonitrile were added. After this was done, a solution of phenyldiazonium chloride, prepared by diazotizing 48 g (0.5 mole) of aniline (35 g of sodium nitrite, 150 ml of water, and 10 ml of concentrated hydrochloric acid), was added drop by drop from a separatory funnel with vigorous stirring. Heat is liberated during the reaction. A piece of ice was therefore placed in the separatory funnel, and the reaction flask was chilled externally with ice, the temperature not being allowed to rise above 30°. After all the solution had been added, stirring was continued, the mixture being warmed to 50-55°, until no more nitrogen was evolved (about 2 hours). Then 200 ml of water was added, the oily layer was separated, the aqueous layer was extracted with ether three or four times and then dried with sodium sulfate, the ether, acetone, and acrylonitrile were driven off, and the residue was distilled in vacuo.

This yielded 23-26 g (i.e., 28-36% of the theoretical) of crude α-chloro-β-phenylpropiononitrile, containing cinnamonitrile as an impurity, since some hydrogen chloride was split out during distillation. B.p. 135-139° at 14 mm. Figures in the literature: b.p. 137-140° at 15 mm [5].

The cinnamonitrile was prepared by refluxing the crude α-chloro-β-phenylpropiononitrile (23 g) with five times its weight of dimethylaniline (115 g). Then the mixture was cooled, and 450 ml of 2N sulfuric acid was added with stirring and chilling. The oily layer was extracted with ether, washed with water, dried with potash, and distilled in vacuo. This yielded 14-15 g, or 77-83% of the theoretical, of cinnamonitrile, containing, apparently, a mixture of the cis and trans isomers. B.p. 113-115° at 15 mm; m.p. 20-22°; n^{25}_{D} 1.5846. Figures in the literature: b.p. 115-120° at 15 mm [5]; 128.8° at 12 mm [6].

Synthesis of α,β-diphenylglutarodinitrile. Six drops of sodium ethylate (1 g of sodium in 20 ml of absolute alcohol) was added to 11.7 g (0.1 mole) of freshly distilled benzyl cyanide. Then the flask was externally water-cooled and its contents stirred while 12.9 g of cinnamonitrile was added a drop at a time. If the mixture did not warm up spontaneously, 2 or 3 more drops of sodium ethylate were added. After addition was complete, the mixture was stirred for another hour at room temperature and for 1.5 hours at 40-50°, after which the reaction mass was poured into a mixture of ice and dilute acetic acid. The precipitate was suction-filtered and recrystallized from alcohol. This yielded 20.0-20.2 g, or 80-82% of the theoretical yield, of pure α,β-diphenylglutarodinitrile. M.p. 105°. The literature gives the m.p. as 101-103° [7].

Synthesis of 3-phenylpiperidine. 8.5 g (0.05 mole) of α-phenylglutarodinitrile was dissolved in 250 ml of n-butyl alcohol, and the solution was heated to 80-90° and then quickly poured over 19 g of metallic sodium (in a flask fitted with a slanting copper condenser). The mixture was heated on an oil bath (150-160°) until the sodium dissolved and then cooled, after which some water was added to decompose the alcohol, and the butyl alcohol and the amine were driven off with superheated steam (up to 180°) and collected in dilute hydrochloric acid. Then the butyl alcohol was separated, the alcoholic layer being washed three times with small portions of water, and the aqueous layer and the wash waters evaporated until crystallization set in. The resultant crude hydrochloride was deeply chilled and then decomposed with pulverized sodium hydroxide, 0.5 g of sodium sulfate being added to the alkali to prevent oxidation of the amine. The layered amine was extracted six or seven times with absolute ether (decantation), the combined extracts (some 150 ml) were dried with fused potassium hydroxide, the ether was driven off, and the residue was distilled in vacuo with a small dephlegmator. This yielded 4.75 g, or 59% of the theoretical yield, of 3-phenylpiperidine. B.p. 121-125° at 12 mm. Redistillation in vacuo in a current of anhydrous nitrogen yielded a b.p. of 125.5-126° at 12 mm; n^{20}_{D} 1.5256; n^{25}_{D} 1.5232; d^{25}_{4} 0.9592; MR_D 51.36. $C_{11}H_{15}N$. Calculated 51.04. The literature gives: b.p. 139-142° at 19 mm [3] and 255-256° at 740 mm [1].

The hydrochloride was secured by passing anhydrous hydrogen chloride through an ether solution of 3-phenylpiperidine. M.p. 143-143.5°. Koelsch [3] gives the m.p. as 143-144°. The picrate and the benzoyl derivatives are oils. The corresponding urethane, i.e., the ethyl ester of N-(β-phenylpiperidyl)-carboxylic acid, was prepared by the action of ethyl chloroformate, using the customary procedure [8]. B.p. 145-146° at 10 mm; n^{25}_{D} 1.5124.

4.805 mg substance: 0.253 ml N_2 (16°, 744 mm). Found %: N 6.09. $C_{14}H_{19}O_2N$. Calculated %: N 6.01.

Synthesis of 3,4-diphenylpiperidine. A solution of 14 g (0.057 mole) of α,β-diphenylglutarodinitrile in 220 ml of n-butyl alcohol was poured over 15 g of metallic sodium. The mixture was heated on an oil bath (180-200°) until the sodium had dissolved (about 45 minutes) and chilled, after which 100 ml of water was added and the mixture was steam-distilled for 4-5 hours, the distillate being collected in a receiver containing hydrochloric acid. The alcoholic layer was separated and washed with water, the aqueous solutions being combined and evaporated until crystallization set in and then decomposed with solid alkali. The amine produced was extracted with absolute ether, the extract being dried with fused potassium hydroxide, the ether driven off, and the residue distilled in vacuo. This yielded 3.0-6.1 g of 3,4-diphenylpiperidine, or 28-45% of the theoretical; the b.p. was 190° at 8 mm. The product crystallized after standing for a long time. M.p. 82-84°. The literature gives: b.p. 230-240° at 23 mm; m.p. 83-84° [3].

SUMMARY

1. Acrylonitrile has been used to synthesize the dinitriles of α-phenylglutaric and α,β-diphenylglutaric acids.

2. A Vyshnegradsky reduction of these dinitriles yielded 3-phenylpiperidine and 3,4-diphenylpiperidine, respectively, their respective yields being 59% and 45% of the theoretical.

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Received July 15, 1950

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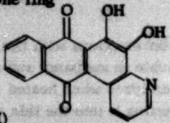
RESEARCHES ON BISULFITE COMPOUNDS

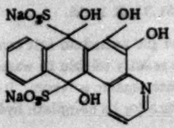
XV. THE STRUCTURE OF THE BISULFITE OF THE DYE ALIZARIN BLUE

V.N.Ufimtsev

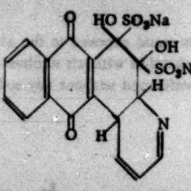
When the dye alizarin blue (I) is treated with sodium bisulfite, an additional product is formed, the dye being employed in dyeing in that form. Graebe and Brunk [1], who were the first to synthesize this compound, (like all later investigators) were unable to isolate it inthe pure state, owing to its low resistance to heat and to the action of alkalies. Only by analyzing the technical product and making a correction for the mineral salt content were they able to establish its empirical formula as $C_{17}H_9NO_4 + 2NaHSO_3$, i.e., as the product of the addition of two molecules of sodium bisulfite to one molecule of alizarin blue. They were unable to establish the structural formula of this compound, confining themselves to suggesting that the bisulfite was added to the nitrogen in the quinoline ring of the dye.

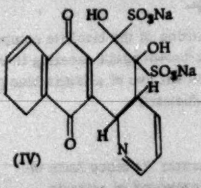
This viewpoint could not be maintained as time went on, since it was difficult to conceive how two molecules of bisulfite could be added to a single nitrogen atom; moreover the bond between the weakly basic nitrogen atom and the bisulfite ought to be hydrolyzed extremely easily by water and be broken down even more readily by the action of strong acids. On the other hand, the formation of the bisulfite compound involves the loss of the ability to form lakes; hence, the reaction affects the alizarin group that is needed for lake formation. That is why the structure of this compound is given in contemporary literature [2] as that of the addition product of sodium bisulfite and the carbonyl groups of the anthraquinone ring (II), without any additional research thereon having been done. When we examine this formula, we note that the carbonyl groups of the anthraquinone ring are not very reactive with the reagents that are typical for other quinones, not reacting, in particular, with bisulfite, as had been established by Graebe and Brunk long ago   in the case of alizarin. In the anthraquinone series, condensation products with bisulfite are yielded only by alizarin blue and its isomer, alizarin green, and their derivatives [3], i.e., by compounds that contain a quinoline ring.


(I)

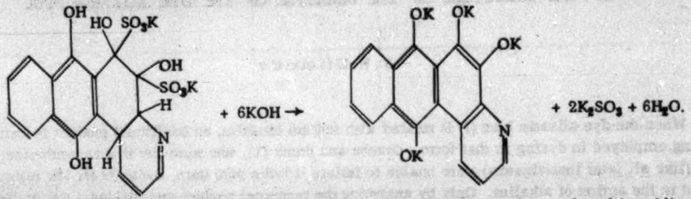

(II)

As has been shown by the researches of Vorozhtsov, Sr. and Kogan [4], the hydroxy derivatives of the quinoline series can react with bisulfite, yielding bisulfite compounds. We therefore assumed that the reaction with bisulfite ought to be similar in the anthraquinone dyes (of the alizarin blue and green type) as well, yielding their bisulfite compounds (III) in the case of alizarin blue and (IV) in the case of alizarin green:


(III)


(IV)

It is not easy to establish the structure of these compounds, as the direct determination of the point at which the bisulfite groups are added is rendered quite difficult by their instability and the failure of their hydroxy groups to enter into acylation reactions (like other bisulfite compounds [5]). We tried to establish their structure by a different approach, proving that the products of the reaction between alizarin blue and bisulfite contain carbonyl groups by reducing them with zinc dust in the cold with acetic acid present. This treatment of a solution of the pure potassium salt of the bisulfite compound we had produced resulted in a sharp change of the solution's color from reddish-brown to yellow. After the zinc dust had been filtered out, boiling the resultant yellow reduced solution readily split off its bisulfite groups, throwing down a brown precipitate of a leuco compound of alizarin blue, which is readily converted into the red vat typical of this dye by the addition of a caustic alkali in the cold with atmospheric oxygen excluded:



The reduced solution is readily reoxidized by atmospheric oxygen, while the vat dye produced is oxidized just as readily to the dye; this is why all this processing must be done with air excluded.

EXPERIMENTAL

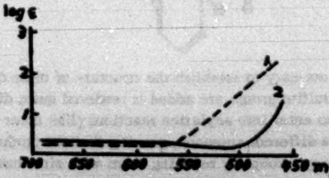
1. Potassium salt of the bisulfite compound of alizarin blue. 20 grams of a commercial 70% paste of the sodium salt of this bisulfite compound was dissolved in the cold in 150 ml of water. A small quantity of activated charcoal was added to the solution, which was then filtered, and 100 ml of a potassium carbonate solution, sp. gr. 1.18, was added. The crystalline precipitate of the potassium salt was filtered out and washed, first with 15 ml of the potassium carbonate solution referred to above, diluted to 50 ml with water, then with 100 ml of methanol, and finally with 50 ml of ether. The synthesized substance weighed 7.2 g after drying in air and then in a vacuum desiccator.

0.5897 g substance: 0.3045 g of pigment dye. 0.1968 g, 0.1367 g, 0.2222 g substance: 0.0610 g, 0.0419 g, 0.0685 g K_2SO_4. Found %: pigment dye 51.64; K 13.91, 13.75, 13.83. $C_{17}H_9NO_4 \cdot 2KHSO_3 \cdot 2H_2O$. Calculated %: pigment dye 51.31; K 13.78.

Under the microscope the potassium salt consists of light-brown prisms with tips cut off at a slant, grouped into hedgehogs; it is readily soluble in water, slightly soluble in methanol and ethyl alcohol, and insoluble in ether or most other organic solvents. It is readily hydrolyzed when heated with water above 60°; 20-30 minutes of boiling suffice for its complete hydrolysis, converting it into the thin violet needles of alizarin blue.

2. Reducing the bisulfite compound of alizarin blue. A 0.00002-molar solution of the potassium salt was prepared by dissolving 0.1135 g of the salt, together with 5 ml of a sodium bisulfite solution, sp. gr. 1.32, and 25 ml of glacial acetic acid, in 2000 ml of water. 5 grams of zinc dust was added to 1000 ml of the resulting solution, and the mixture was agitated briefly and then quickly filtered on a Buchner funnel. During this processing the initial reddish-brown color of the solution changed rapidly to bright-yellow, which is the color of the leuco compound of the bisulfite alizarin blue. The spectra of the solution before and after reduction were photographed with a Goldberg spectrodensometer: the absorption of the initial solution of the bisulfite compound begins at 560 mμ and continues into the ultraviolet region; the absorption of its leuco compounds starts at about 490 mμ.

When the reduced solution of the bisulfite compound was allowed to stand exposed to the air, it oxidized rapidly, turning reddish-brown again; treating it with solid sodium hydroxide with air excluded colors it the characteristic red of the vat dye of alizarin blue (this reaction was performed without any sodium bisulfite being added before reduction).



Absorption spectra: 1) leuco form of the bisulfite compound of alizarin blue; 2) bisulfite compound of alizarin blue.

SUMMARY

1. The potassium salt of the bisulfite compound of alizarin blue has been secured in the pure state and its conversion into the leuco form when reduced has been established.

2. The spectrum curves of the bisulfite compound and of its leuco form have been plotted, and formulas for their structure as products of the reaction of bisulfite with their hydroxy groups are put forward.

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Received August 14, 1950.

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RESEARCH ON SULFONATION

XXII. SYNTHESIS OF NAPHTHALENE TRISULFOCHLORIDES

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We have previously described the synthesis of 1,3,5-naphthalene trisulfochloride by the action of chlorosulfonic acid upon 1,5-naphthalene disulfochloride. The present paper describes the sulfonation of five other naphthalenedisulfochlorides by the same methods and some results of our exploration of this reaction.

As we know, the sulfonation of naphthalene or of the sulfo acids produced by the direct sulfonation of naphthalene yields three isomeric trisulfo acids. Since the information in the literature on the synthesis of 1,3,5-naphthalenetrisulfonic acid has been cited previously [1], we supply below only the information on the synthesis of the 1,3,6- and 1,3,7-trisulfo acids.

Armstrong and Wynne [2] synthesized the 1,3,6-trisulfo acid, identified as the trichloride with the m.p. 194°, by reacting naphthalene with chlorosulfonic acid. Friedlander [3] notes that almost nothing but the 1,3,6-trisulfo acid is produced when the 1,6- and 2,7-disulfo acids are sulfonated. The synthesis of the 1,3,7-trisulfo acid is described in a German patent [4]. The 2,6-disulfo acid was sulfonated on a water bath with oleum, containing 2.2 moles of the free anhydride per mole of the disulfo acid. Fierz-David [5] described two ways of synthesizing the 1,3,6-trisulfo acid. In the first method, naphthalene is first sulfonated by the monohydrate to the β-monosulfo acid at 165°, and then to the 1,6-disulfo acid with 60% oleum (3.4 moles of the anhydride per mole of naphthalene), at 50° to begin with and then at 165°. In the second method, the naphthalene is first sulfonated to the 2,7-disulfo acid with the monohydrate at 165°, and then with oleum (3.15 moles of SO_3 per mole of naphthalene) at 125-170°. Ufimtsev and Krivoshlykova [6] modified the first method described by Fierz-David somewhat, adding the oleum in two batches. After the first batch of oleum was added, sulfonation and rearrangement of the remainder of the disulfo acids took place at 155°, the second batch of oleum then being used for sulfonation. This raised the yield of the 1-amino-3,6,8-trisulfo acid (T acid) from 62 to 68%. A new method of producing the 1,3,6-acid has been developed at the Dorogomilovo plant [7], consisting of the following: the naphthalene was sulfonated to the 1,5-disulfo acid, after which rearrangement was effected at various temperatures, and exhaustive sulfonation was effected with oleum. The yield of the T acid in the nitro mass was 70%. Vorozhtsov and Chuksanova [8] sulfonated the 1,6-disulfo acid in the air and secured 80% of the theoretical yield of the 1,3,6-acid, the yield rising to 95% when the apparatus used was filled with nitrogen. Fierz-David and Richter [9] found that 87-92% of the 1,3,6-trisulfo acid and about 4% of other trisulfo acids were produced when 1,6- and 2,7-naphthalenedisulfo acids were sulfonated with an excess of oleum for 10 hours at 160°. These results indicate that at this temperature the di- or trisulfo acids are largely isomerized in fuming sulfuric acid, and that it is impossible to secure a pure trisulfo acid from the pure disulfo acids.

Thus, chlorosulfonic acid has never been used in sulfonation to produce naphthalene trisulfochlorides, and the trisulfo acids were never produced without traces of other isomers.

It is shown in the present paper that when the pure acid chlorides or salts of the 1,6- and 2,7-disulfo acids are processed with chlorosulfonic acid, pouring the reaction mixture out over ice yields the pure 1,3,6-trisulfochloride without any further refining. Similarly, the 2,6-disulfochloride yields the pure 1,3,7-trisulfochloride.

The results of our experiments on the chlorosulfonation of 1,6- and 2,7-naphthalene disulfochlorides set forth in Table 1 show that a highly pure 1,3,6-trichloride with a melting point that is at times as high as 197° is produced. (The highest melting point of 198° for the 1,3,6-trichloride was found by Ufimtsev and Krivoshlykova [6]). The reaction was not complete in Experiment 150, since the resultant trichloride was converted into a product with a m.p. of 195-195.5° when it was reprocessed with chlorosulfonic acid for 2 hours

TABLE 1

Synthesis of 1,3,6-Naphthalene Trisulfochloride From the 1,6- and 2,7-Dichlorides

Test No.	Used		Reaction temperature	Time, hours	Yield of the 1,3,6-trichloride, per cent of the theoretical	Melting point of the resultant trichloride
	Disulfochloride	Moles of HSO$_3$Cl per mole of the chloride				
424	1,6-	4.7	125°	4	69.0	193-195°
145	1,6-	9.5	124	6	82.8	193-195
166	1,6-	10.2	149	1	82.7	194-195
110	1,6-	10.4	123	3	91.9	193.5-194
123	1,6-	14.3	125	3	85.5	194-195
125	1,6-	14.3	125	3	87.5	195-196
128	1,6-	20.1	125	3	94.4	194-195
394	2,7-	5	126	3	70.5	196-197
416	2,7-	4.9	125	6	72.8	193-195
149	2,7-	9.2	124	6	86.3	193.5-194
167	2,7-	10.2	149	1	85.2	195.5-196.5
148	2,7-	10.1	100	6	90.0	193.5-194
150	2,7-	14.4	100	2	91.9	188-191
46	2,7-	14.9	125	3	90.7	194-195
56	2,7-	14.5	125	3	92.5	194-195

at 100°. The yield of the trichloride ranges from 70 to 94% of the theoretical, depending on the amount of the excess and the quality of the chlorosulfonic acid. As has been reported previously [1], the chlorosulfonic acid, distilled in vacuo, contains a small amount of sulfuric acid, so that when it is sulfonated the yields of the trichloride are somewhat lower than the yields obtained when acid distilled at ordinary pressure is employed. What is more, using repeatedly distilled chlorosulfonic acid raises the yield of the trichloride.

TABLE 2

Chlorosulfonation of 2,6-, 1,7-, and 1,3-Naphthalene Disulfochlorides

Test No.	Used		Reaction temperature	Time, hours	Yield of trichlorides, per cent of the theoretical	Melting point of the resultant trichloride
	Disulfochloride	Moles of HSO$_3$Cl per mole of the chloride				
112	2,6-	5.2	124°	6	69.1	163-165°
168	2,6-	10.2	149	1	77.5	163-164
108	2,6-	10.2	124	3	85.3	164-165
126	2,6-	14.6	125	3	91.5	164-165
44	2,6-	14.8	125	3	92.8	164-165
156	1,7-	14.5	100	4	85.4	126-139
160	1,7-	14.7	100	6	85.8	128-140
170	1,7-	20.4	100	8	90.5	130-142
169	1,7-	18.4	149	1	82.9	134-144
462	1,7-	32.1	146	1/2	86.1	135-144
45	1,7-	38.2	148	3	89.3	137-144
97	1,3-	16.8	150	3	97.1	115-128
463	1,3-	17.7	140-148	20 min.	81.0	120-125

The results of our experiments on the sulfonation of the 2,6-disulfochloride, given in Table 2, indicate that the 1,3,7-trisulfochloride secured is likewise highly pure (the highest melting point given in the literature for the 1,3,7-trichloride is 166°), its yield depending upon the amount of excess chlorosulfonic acid used and its quality.

Table 2 also gives the results of our experiments on the sulfonation of 1,7- and 1,3-naphthalene disulfochlorides. When the 1,7-dichloride is sulfonated, the sulfo group may be attached at the 3 or 5 position, yielding the 1,3,5- and 1,3,7-trisulfochlorides. As the 5 position is more reactive than the alpha position, the 1,3,5-isomer is produced with a low percentage of the 1,3,7-isomer, the resultant product having a melting point that is only a few degrees below that of the pure 1,3,5-trichloride. Our tests also indicated that less of the 1,3,7-isomer is produced at 146-148° than at 100°.

All three of the trisulfochlorides can be produced from the 1,3-disulfochloride, with the 1,3,5-isomer again predominating in the mixture apparently. The melting point of the product indicates, however, that appreciable percentages of the two other isomers are present.

TABLE 3

Synthesis of Naphthalene Trisulfochlorides From Sodium Salts of Disulfo Acids and Once-Distilled HSO_3Cl

Test No.	Used		Reaction temperature	Time, hours	Yield of trichlorides, per cent of the theoretical	Melting point of the resultant trichloride
	Salt of the disulfo acid isomer	Moles of HSO_3Cl per mole of chloride				
172	1,5-	25.3	149°	2	63.2	145-146°
171	1,6-	25.4	149	2	78.8	194-194.5
139	2,7-	29.4	124	6	61.3	195-196

Pure trisulfochlorides are produced when the sodium salts of the disulfo acids as well as the disulfochlorides are chlorosulfonated. The results of our experiments on the chlorosulfonation of the sodium salts of the 1,5-, 1,6-, and 1,7-disulfo acids, listed in Table 3, indicate that these trisulfochlorides are no less pure; their yields are much lower, however, than the yields secured when the disulfochlorides are sulfonated. The reason for the low yields of chlorides from the salts of sulfo acids have been set forth earlier [10].

We know that when sulfuric acid, oleum, and frequently even chlorosulfonic acid are used in sulfonation, by-products are obtained, the sulfomixture containing sulfones, resins, products of higher sulfonation, isomeric sulfo acids, and the unsulfonated initial product, in addition to the excess of the sulfonating agent. Hence the recovery and refining of the reaction product are often very troublesome operations. No sulfones, resins, and tetrasulfochloride are formed when the sodium salts of naphthalenedisulfonic acids and their acid chlorides are sulfonated with chlorosulfonic acid, nor is any unreacted disulfo derivative left.

We know that when 1,6- and 2,7-disulfo acids are sulfonated with oleum at 160°, the disulfo acids or the resultant trisulfo acid are isomerized appreciably [9]. No isomerization of the sulfo acids was found in our experiments. In most cases, however, we recovered far from all the trisulfo acid as a chloride. It may be assumed that the free sulfo acid in the reaction mixture can be isomerized, the resulting isomers remaining in the solution after the reaction mixture has been poured over ice. To test this assumption, we ran experiments on the sulfonation of the 1,5-dichloride at 149°, the results being set forth in Table 4. When the reaction time was brief and the excess of the chlorosulfonic acid was small, we sometimes got a product containing a trace of the unreacted 1,5-dichloride, as indicated by its melting point. After the chloride had been precipitated, the aqueous solution, which contained sulfuric and hydrochloric acids, was evaporated on a water bath to constant weight in order to eliminate the latter acid, after which it was diluted with water and neutralized with barium carbonate, the barium sulfate being filtered out. The barium salts of the sulfo acids in the solution were converted into sodium salts with soda, the barium carbonate being filtered out, the filtrate evaporated to dryness, and the sodium salts converted into the acid chlorides.

The last columns in Table 4 give the percentages of the trichloride secured from the sulfo acid and its melting point. The experimental results show that the melting point of the trichloride produced initially is the same as that of the trichloride secured from the sulfo acids that remained in the filtrate when the reaction mixture was decomposed. This indicates that the sulfo acids are not isomerized when disulfo derivatives of naphthalene are chlorosulfonated at 150° for 6 hours. Moreover, if the reaction mass does contain a mixture of isomeric sulfo derivatives (or of di- and tri-derivatives), the composition of the mixture of isolated chlorides does not differ from that of the mixture of free sulfo acids dissolved in water when the reaction mass is decomposed.

It was noted earlier [1] that the rate of sulfonation with chlorosulfonic acid depends on how much of an excess of the acid is used. The more chlorosulfonic acid is employed per mole of the dichloride, the sooner the

TABLE 4

Conversion of the 1,5-Dichloride Into the Trichloride and Analysis of the Filtrate After the Trichloride Had Been Precipitated by Pouring the Reaction Mixture Over Ice

Test No.	Moles of HSO_3Cl used per mole of the 1,5-dichloride	Reaction time, hours	Temperature	1,3,5-Trichloride Produced				Total yield, per cent of the theoretical
				Precipitated on Ice		From the filtrate via the sodium salt		
				Per cent of the theoretical	Melting Point	Per cent of the theoretical	Melting Point	
24	2.35	0.5	149°	59.5	127-134°	21.3	129-134°	80.8
18	4.70	0.5	148	67.4	140-141	21.9	140-141.5	89.3
22	7.82	0.5	148	81.9	146	8.4	145.5-146	90.3
27	2.36	4	149	40.1	144	54.5	144	94.6
23	7.82	6	149	77.8	144-144.5	14.1	144	91.9

formation of the trichloride is complete. The experimental results given in Table 5 show whether this depends upon the dilution of the chlorosulfonic acid by the sulfuric acid produced in the reaction or only upon the amount of chlorosulfonic acid active. The 1,5-dichloride was sulfonated with chlorosulfonic acid that had been distilled in vacuo, with and without the addition of 100% sulfuric acid. The results of six experiments, performed in pairs with all other conditions remaining the same, showed that the melting point of the product synthesized was practically the same in both cases, evidence of the identical proportions of the residual unsulfonated dichloride and the resultant trichloride. Hence, the rate of sulfonation depends upon the excess of chlorosulfonic acid used and not upon the percentage of sulfuric acid it contains (which ranges from 1 to 12% at most).

TABLE 5

Chlorosulfonation When the Chlorosulfonic Acid Contains Sulfuric Acid

Test No.	Moles of HSO_3Cl used per mole of the 1,5-dichloride	Per cent of H_2SO_4 in the HSO_3Cl	Reaction Temperature	Time, Minutes	Yield of the 1,3,5-trichloride, per cent of the theoretical	Melting point of the synthesized trichloride
175	7.19	1.0	100°	30	74.3	138-158°
176	7.24	11.6	100	30	61.5	135-159
91	7.54	1.5	125	20	76.7	136-140
90	7.42	10.6	125	20	63.6	135-139
86	7.54	2	125	60	77.4	145-145.5
87	7.49	10.9	125	60	61.8	145-145.5

We have shown earlier [1] that adding phosphoric anyhydride during the sulfonation of 1,5-naphthalene disulfochloride with chlorosulfonic acid raises the yield of the trichloride, due to the formation of pyrosulfuryl chloride ($S_2O_5Cl_2$) in the reaction mixture. The results of our experiments on sulfonation of the 1,5-dichloride with pyrosulfuryl chloride alone, prepared according to [11], and with a mixture of pyrosulfuryl chloride and chlorosulfonic acid, are given in Table 6. These experiments showed that pyrosulfuryl chloride by itself sulfonates much more slowly than does the chlorosulfonic acid. Experiment 83, for example, indicated that only a small portion of the dichloride was sulfonated in 3 hours at 125°, as shown by the melting point of the reaction product. Sulfonation for 12 hours did not yield a pure product, while prolonging the reaction time to 24 hours did not raise the melting point of the trichloride, but lowered it (Experiments 106 and 114). Hence, the action of pyrosulfuryl chloride also involves side reactions, their products contaminating the resultant trichloride. This is likewise shown by the results of Experiments 107 and 115.

Sulfonation with chlorosulfonic acid to which pyrosulfuryl chloride has been added yields much better results than sulfonation with chlorosulfonic acid or pyrosulfuryl chloride alone. The results of Experiment 94, for instance, indicated that 8.4 moles of chlorosulfonic acid plus 0.85 mole of pyrosulfuryl chloride produce a nearly quantitative yield of the trichloride, whereas the same yield requires no less than 25 moles of chlorosulfonic acid per mole of the dichloride when only the chlorosulfonic acid is used [1]. Similarly, 4.2 moles of chlorosulfonic acid plus 0.44 mole of pyrosulfuryl chloride give the same yield as secured with 10 moles of the chlorosulfonic acid alone.

TABLE 6

Chlorosulfonation with Pyrosulfuryl Chloride Alone and Mixed with HSO_3Cl.

Test No.	Moles used per mole of the 1,5-dichloride		Reaction temp.	Time, hours	Yield of the 1,3,5-trichloride, % of theoretical	M.p. of the synthesized trichloride
	HSO_3Cl	$S_2O_5Cl_2$				
83	-	5.06	125°	3	-	148-161°
106	-	4.94	125	12	90.7	141-142
114	-	5.20	125	24	95.4	137-139
107	-	2.54	125	24	92.3	141-142
115	-	2.56	125	48	88.9	135-139
85	4.29	0.45	125	3	86.1	142-143
106	4.21	0.44	125	6	85.6	145-146
94	8.43	0.86	125	6	98.7	145-146

All the experiments on the synthesis of the trichlorides were run in the same way as described in the previous report [1].

P. T. Pestova participated in this research.

SUMMARY

When the acid chlorides of 1,6- and 2,7-naphthalenedisulfonic acids or their sodium salts are sulfonated with chlorosulfonic acid, we get pure 1,3,6-naphthalene trisulfochloride after the mixture is decomposed on ice. Pure 1,3,7-naphthalene trisulfochloride is also secured from 2,6-naphthalene disulfochloride; the 1,3- and 1,7-dichlorides yield a mixture of trichlorides.

No isomerization of the naphthalenedi- or trisulfonic acids or of their chlorides occurs in chlorosulfonic acid at any temperature up to 150°, that is, up to their boiling point.

A given mixture of chlorides in chlorosulfonic acid containing sulfuric acid is partially converted into a mixture of the sulfo acids having the same composition as the mixture of chlorides.

The presence of sulfuric acid (up to 12%) in the chlorosulfonic acid has no effect upon its sulfonation rate.

Sulfonation with pyrosulfuryl chloride is much slower than sulfonation with chlorosulfonic acid.

The presence of about 0.1 mole of pyrosulfuryl chloride per mole of chlorosulfonic acid results in a considerable increase in the product yields during sulfonation.

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Received July 10, 1950.

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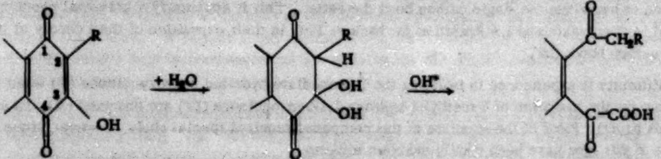
OXIDATIVE AND OXIDATIVE-HYDROLYTIC TRANSFORMATIONS OF ORGANIC MOLECULES

XXI. HYDROLYTIC CLEAVAGE OF 6-METHYL-3-HYDROXY-1,4-BENZOQUINONE*

L. A. Shchukina

During the past few years M.M.Shemyakin, together with the present author and other collaborators, has developed and laid the experimental underpinning for a theory of the oxidative-hydrolytic transformations of organic molecules [1-20], which makes possible a new approach to the cleavages of carbon bonds that occur when oxidative and hydrolyzing agents act together or consecutively.

In one of our preceding reports [19] it was shown, in connection with the relationship existing between the degree of oxidation of carbocyclic compounds and the ability of their ring groups to undergo hydrolytic cleavage, that hydroxyquinones of Type (I), which contain a hydrogen atom or an alkyl radical at the 2 position, ought to be cleaved readily, because of their structural peculiarities, when hydrolyzing agents are present, as follows:



(I) (II) (III)

R = H or Alk.

Up to the present time, however, the feasibility of this reaction has been established only for the respective naphthalene and phenanthrene hydroxyquinones, viz.; 3-hydroxy-1,4-naphthoquinone, 2-methyl-3-hydroxy-1,4-naphthoquinone, 2-hydroxy-1,4-phenanthrenequinone, and 3-hydroxy-1,4-phenanthrenequinone, which are readily cleaved hydrolytically in accordance with the foregoing schema [3,4,21]. As for the analogous hydroxyquinones of the benzene series, no research has yet been done on the conditions and nature of the hydrolytic cleavage of their ring groups. We were therefore interested in exploring this problem, using one of the simplest representatives of the hydroxybenzoquinones, in order to show that the reaction in question applies to all the Type (I) hydroxyquinones, no matter to what series they belong. Research on the hydroxybenzoquinones is also of interest from the biochemical standpoint, since M.M.Shemyakin believes that the phenylalanine–tyrosine interchange within the organism, involving the cleavage of their aromatic rings, probably occurs as follows: these amino acids are first oxidized to quinolylalanine and then to hydroxyquinolylalanine the ring grouping of which is then cleaved hydrolytically. Inasmuch as 6-methyl-3-hydroxy-1 4-benzoquinone (IV) is fairly close to quinolyl- and hydroxyquinolylalanine, among the simplest benzene hydroxyquinones, we chose this hydroxybenzoquinone as the first object of our investigation.

As was to have been expected on the basis of the theoretical considerations set forth previously [19], 6-methyl-3-hydroxy-1,4-benzoquinone (IV) proved that it could be first hydrated (with and without atmospheric oxygen present) and then cleaved hydrolytically in accordance with the equation below, it being found that the conditions required for this process are much milder than for the corresponding hydroxynaphtho- and hydroxyphenanthrenequinones: ** (see following page).

Hence, the hydrolytic cleavage in question is actually common to all Type (I) hydroxyquinones, no matter whether they belong to the benzene, naphthalene, or phenanthrene series.

Another significant fact is that 6-methyl-3-hydroxy-1,4-benzoquinone (IV) is hydrated more easily than the intermediate compound (V) is cleaved hydrolytically. This made it possible to divide the process into two stages,

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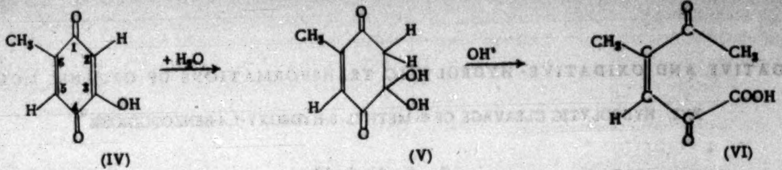
*) Report XIII on the hydrolytic cleavage of carbon bonds.

**) Compare the experimental findings set forth in the present report with those described in the articles [3, 14, 21].



isolating the hydrated hydroxyquinone (V), which proved to be a quite stable compound. The isolation of this substance serves as experimental proof of the mechanism of hydrolytic cleavage of Type (I) hydroxyquinones previously advanced by M.M.Shemyakin and the present author [1,3,14,19], which has been merely a hypothesis up to now. On the other hand, the isolation of the intermediate hydrated hydroxyquinone (V) enabled us to make a separate study of each of the stages involved in the conversion of the initial 6-methyl-3-hydroxy-1,4-benzoquinone (IV) into the final diketocarboxylic acid (VI). We found that the first stage – hydration – can be carried out by heating an aqueous solution of 6-methyl-3-hydroxy-1,4-benzoquinone, whose initial pH is 7, to 37° for 48 hours. The second stage – the hydrolytic cleavage of the hydrated hydroxyquinone (V) to the diketocarboxylic acid (VI) – takes place only when the solution pH exceeds 7, the process being quantitative when a 0.1 N aqueous solution of alkali is present, concluding within half an hour at 20°; when the solution pH is 9.17, the process requires 72 hours of heating to 37°. It is therefore beyond doubt that it is easier to hydrate the double bond in the 6-methyl-3-hydroxy-1,4-benzoquinone molecule than to hydrolyze the single carbon bond thereafter. This is apparently a universal phenomenon, as was stressed by M.M.Shemyakin and I.A.Redkin as far back as 1941 in their exposition of their theory of the hydrolytic cleavage of carbon bonds [22].

No difficulty is experienced in isolating the intermediate hydrated hydroxyquinone (V) when the conditions outlined above for the hydration of 6-methyl-3-hydroxy-1,4-benzoquinone (IV) are observed (see the experimental section of this paper). Proof of the structure of this compound required special study, however, since hydrated hydroxyquinones of this type have been wholly unknown hitherto.

In contrast to the bright-yellow initial hydroxyquinone (IV), the product of its hydration (V) we isolated is a white crystalline substance that fused with decomposition at 234°. The analytical data and the results of our determination of the molecular weight of this compound indicate an empirical formula of $C_7H_8O_4$, which is evidence that one molecule of water has been added to the molecule of the original hydroxyquinone. This water cannot be eliminated by recrystallizing the substance from organic solvents or by drying it in vacuo at 5 mm; the only way the elements of water can be removed is by using concentrated sulfuric acid or by subliming the substance in vacuo (280-300° at 5 mm), 6-methyl-3-hydroxy-1,4-benzoquinone (IV) being produced in both instances. These findings indicate that the compound we have isolated is not a crystal hydrate and that it possesses the carbon ring skeleton of the original hydroxyquinone.

These facts are not enough, however, to resolve the problem of the position at which the elements of water are added to the molecule of 6-methyl-3-hydroxy-1,4-benzoquinone (IV), as the latter can be hydrated either at the $>C=C<$ double bond or at the $>C=O$ double bond. Inasmuch as the hydration product would have to contain two hydroxyl groups in the former case and three in the latter, the solving of this problem may be reduced to a determination of the number of hydroxyl groups in the molecule of our synthesized compound. We found that this substance possesses only two active hydrogen atoms, while a diacetyl derivative, rather than a triacetyl one, is produced when it is acetylated with acetic anhydride in the presence of sulfuric acid. This demonstrates that when the hydroxyquinone (IV) is hydrated, the elements of water are added at one of the double bonds of the quinone ring rather than at the carbinol group.

There remains to consider the question of which of the ring's double bonds (the 2,3 or the 5,6 bond) undergoes hydration. As has been stated above, we secured a quantitative yield of nothing but a diketocarboxylic acid when we cleaved the hydrated hydroxyquinone hydrolytically. The only way in which that acid can be formed is by the hydroxyl group entering the quinone ring at the 3 position when the original hydroxyquinone is hydrated, with the hydrogen atom entering at the 2 position, inasmuch as any other order of addition of the elements of water would result in the formation of polycarbonyl compounds as the hydrolysis end products instead of the diketocarboxylic acid we recovered. There is, therefore, no doubt that the product of the hydration of 6-methyl-3-hydroxy-1,4-benzoquinone has the structure represented by Formula (V).

The diketocarboxylic acid produced in the hydrolytic cleavage of the compound (V) is not described in the literature. It is a white crystalline substance that melts with decomposition at 258°; it crystallizes from water with 1.5 molecules of the solvent, after which it fuses at 203° with decomposition. The data of the analysis of the anhydrous acid and the results of a determination of the molecular weight of one of its derivatives (see the experimental section of this paper) indicate that this acid has the empirical formula of $C_7H_8O_4$. Hence, this acid is an isomer of the hydrated hydroxyquinone (V). The presence of a single carboxyl group in its molecule was established by titrating the acid directly with an alkali solution; we also secured the corresponding p-nitrobenzyl ester. The latter, as well as the acid itself, yields mono-p-nitrophenylhydrazones.

When the acid we had synthesized was heated with ammoniacal silver nitrate, a silver mirror was formed, due to the presence of the $-CO-COOH$ group in its molecule. Iodoform was produced by the action of an alkaline hypoiodite solution upon the acid; this is evidence of the presence of a $-CO-CH_3$ group, whence it follows that the acid in question is an acyclic compound. These findings indicated that the acid contains two active hydrogen atoms, one belonging to the carbonyl group, and the other to the $-CO-CH_3$ group.

Thus we have shown that all the three groups that were to be expected in the acid in question on the basis of its hypothetical structure are actually present in it. In the light of the conditions governing its formation and the structure of the initial compounds (IV) and (V), it is certain that this acid has the structure represented by Formula (VI).

EXPERIMENTAL*

Synthesis of 6-methyl-3-hydroxy-1,4-benzoquinone. We synthesized this quinone by the method described by Thiele and Winter [23]. This method consists of the following three stages: 1) acetylating toluquinone with acetic anhydride in the presence of sulfuric acid; 2) saponifying the resulting 2,4,5-triacetoxytoluene to 2,4,5-trihydroxytoluene with sulfuric acid in methanol; and 3) oxidizing the trihydroxytoluene to 6-methyl-3-hydroxy-1,4-benzoquinone (IV) with ferric chloride.

The first stage of this synthesis involved no difficulty, the yield of the 2,4,5-triacetoxytoluene, with a m.p. of 114-115° (from methanol) being 70%. But when we endeavored to reproduce the second and third stages, we either failed to obtain the end product (IV) entirely or else its yield was negligible. We were therefore obliged to modify the reaction conditions somewhat, enabling us to secure a 50% yield of the 6-methyl-3-hydroxy-1,4-benzoquinone, based on the 2,4,5-triacetoxytoluene. The modified procedure used to secure this quinone is set forth below.

120 grams of methanol, 4 g of concentrated sulfuric acid, and 100 g of 2,4,5-triacetoxytoluene were placed in a round-bottomed flask fitted with a reflux condenser. The resultant solution was boiled for 45 minutes, after which the reaction mass was cooled, 4.5 g of calcined soda was added to it, and 75-80 ml of the methanol was driven off. The residue was poured into 100 ml of a saturated aqueous solution of sodium sulfate and extracted 4 times with ethyl acetate. The ethyl acetate solution was dried with sodium sulfate, after which a large part of the solvent was driven off. The remaining liquid, which was still mobile, was transferred to a porcelain dish and evaporated to a thick brown syrup, which crystallized in part upon cooling. The resulting 50 g of 2,4,5-trihydroxytoluene can be oxidized to 6-methyl-3-hydroxy-1,4-benzoquinone (IV) without preliminary refining.

This was done by dissolving 50 g of the 2,4,5-trihydroxytoluene in 50 ml of a saturated solution of sodium chloride and dissolving 140 g of anhydrous ferric chloride in 280 ml of a 15% aqueous solution of sodium chloride, after which the first solution was poured into the second rapidly, with very vigorous stirring. The yellow hydroxyquinone (IV) was precipitated nearly instantaneously; it was rapidly filtered out on a Buchner funnel 1 to 2 minutes later. The precipitate was pressed out, washed with 20 ml of a saturated solution of sodium chloride, and immediately transferred, together with the filter, to a beaker containing 200 ml of ether. The aqueous layer was separated, the ether solution was dried with sodium sulfate, and the ether was driven off. The residue was recrystallized from benzene. This yielded 27 g of 6-methyl-3-hydroxy-1,4-benzoquinone, which fused at 142° with decomposition. The yield was 52%, based on the 2,4,5-triacetoxytoluene.

Hydration of 6-methyl-3-hydroxy-1,4-benzoquinone. 10 g of 6-methyl-3-hydroxy-1,4-benzoquinone was dissolved in 3 liters of distilled water at 37°, and the solution was kept in a thermostat at that temperature for 48 hours. After heating was over, 1 g of activated charcoal was added to the reaction solution, which contained a small amount of a tarry deposit, and the solution was allowed to cool to room temperature. Then the precipitate was filtered out, and the solution was evaporated to dryness in vacuo, at 40° and 10 mm.** The residue was washed twice in the flask with a small amount of ether, after which it was mixed with 10 ml of water, filtered out, and washed on the filter with 3 ml of water. The resultant white crystalline substance (5 g) was recrystallized from water containing activated charcoal. It was the hydrated hydroxyquinone (V), which crystallized from water in well-shaped rhombohedrons. After the substance had been dried in vacuo (100° and 5 mm) to constant weight, it fused at 234° with decomposition (first turning dark). The yield was 3.4 g, or 30%.

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*) We are indebted to E. A. Ignatyeva, who assisted in the analytical portion of the research

**) Violent frothing was observed during evaporation; it was eliminated by adding small quantities of octyl alcohol.

This compound is rather freely soluble in water, methanol, ethyl alcohol, acetone, and hot acetic acid, and sparingly soluble in ether.

Found %: C 53.97; H 5.08. M 158 (in dioxane). $C_7H_8O_4$. Calculated %: C 53.84; H 5.13; M 156.

The number of active hydrogen atoms (determined in pyridine by the Terentyev method) was 1.96 and 2.15.

Conversion of the hydrated hydroxyquinone (V) into the original hydroxyquinone (IV). a) 0.2 g of the hydrated hydroxyquinone (V) was dissolved in 3 ml of concentrated sulfuric acid. Three minutes later, the dark-red solution was poured into 150 ml of water and extracted 5 times with ether. The ether extract was extracted four times with a 10% solution of sodium bicarbonate, then acidulated with an aqueous solution of 20% sulfuric acid, and extracted several times with ether. The ether solution was dried with sodium sulfate, the ether driven off, and the residue washed with a few drops of ether. The resultant yellow crystalline substance fused at 140-142° and exhibited no depression of the mixed melting point with 6-methyl-3-hydroxy-1,4-benzoquinone. The yield was 25%.

b) 0.2 g of the hydrated hydroxyquinone (V) was sublimed in vacuo at 5 mm and 280-300°. The yellow crystalline sublimate was dissolved in ether, the 6-methyl-3-hydroxy-1,4-benzoquinone being recovered from the ether solution as described in Experiment (a). The quinone yield was 21%; m.p. 140-142°.

Acetylating the hydrated hydroxyquinone (V). 0.5 g of the hydrated hydroxyquinone (V) was added to 3 ml of acetic anhydride containing one drop of concentrated sulfuric acid; the substance did not dissolve completely. The next day the precipitate was filtered out and washed with alcohol. The resultant diacetyl derivative did not fuse when heated to 330°. Weight: 0.65 g; yield: 85%. This compound is sparingly soluble in alcohol, acetone, dioxane, nitrobenzene, and other organic solvents. It can be recrystallized from acetic anhydride, from which it settles out as rhombic crystals.

Found %: C 55.14; H 5.20. $C_{11}H_{12}O_6$. Calculated %: C 55.00; H 5.00.

The number of acetyl groups in the synthesized compounds was determined as follows. A sample of the substance (about 0.15 g) was placed in 3 ml of concentrated sulfuric acid. Two or three minutes later 25 ml of water was added to the dark-red solution, and the resulting acetic acid was driven off with steam; its percentage in the distillate was determined by titration with a 0.1 N alkali solution. The number of acetyl groups was found to be 2.03 and 2.12 by this method.

Hydrolytic cleavage of the hydrated hydroxyquinone (V). a) Cleavage with a 0.1 N alkali solution. 1.0 gram of the hydrated hydroxyquinone (V) was dissolved in a quantity of 130 ml of aqueous sodium hydroxide, and the colorless solution was allowed to stand for 30 minutes at 20°. Then 20 ml of 1 N sulfuric acid and 15 g of sodium sulfate were added, and the solution was evaporated to dryness in vacuo at 40° and 5 mm.[*] The dry residue was extracted with ether in a Soxhlet apparatus for 24 hours. Then the ether solution was evaporated to about 5 ml volume and the precipitated diketocarboxylic acid (VI) was filtered out. Decomp. temperature 258°. Yield: 0.1 g, or 100%.

Similar results were secured when this experiment was carried out in nitrogen.

The substance was recrystallized from 2 ml of water, from which it settled out as elongated white lamellae that contained 1.5 molecules of crystallization water. The crystal hydrate fused at 201-203° with decomposition after it had been air-dried.

Found %: C 45.67; H 6.12; M 184 (titration with 0.1 N alkali). $C_7H_8O_4 \cdot 1.5\ H_2O$.
Calculated %: C 45.90; H 6.01; M 183.

The crystallization water was eliminated by drying a sample of the substance in vacuo at 110° and 5 mm to constant weight. The decomposition temperature of the anhydrous acid was 258°.

Found %: H_2O 14.58. $C_7H_8O_4 \cdot 1.5\ H_2O$. Calculated %: H_2O 14.67.

Results of analysis of the anhydrous acid: Found %: C 53.86; H 5.12; M 158 (titration with 0.1 N alkali). $C_7H_8O_4$. Calculated %: C 53.84; H 5.13; M 156.

Number of active hydrogen atoms (determined in pyridine by the Terentyev method): 1.88.

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[*] In this and other instances the sodium sulfate has to be added to effect more complete and satisfactory extraction of the dry residue from the flask after the water has been driven off in vacuo.

Both the aqueous and the anhydrous diketocarboxylic acid (VI) are freely soluble in water, methanol, ethyl alcohol, glacial acetic acid, and dioxane. When treated with ferric chloride it turns an intense brown; it does not decolorize bromine water. It forms a silver mirror only when heated with ammoniacal silver nitrate.

b) Cleavage in a buffer solution at pH 9.17. 1 g of the hydrated hydroxyquinone (V) was dissolved in 200 ml of aqueous disodium phosphate (pH 9.17; buffer capacity 0.1 mole), and the resultant solution was left in a thermostat for 72 hours at 37°. After the reaction was over, the solution was acidulated with 20% sulfuric acid until the pH = 1, after which the phosphoric acid was precipitated with calcium carbonate. The precipitate was filtered out and thoroughly washed with water, the filtrate being acidulated with sulfuric acid until its reaction with Congo red was acid and then evaporated to dryness in vacuo at 40° and 10 mm without filtering out the precipitated calcium sulfate. The dry residue was extracted with ether in a Soxhlet apparatus for 24 hours. Driving off the ether left an oily substance, containing phosphoric acid, which was dissolved in 50 ml of water, after which the phosphoric acid was reprecipitated with calcium carbonate. The precipitate was filtered out and washed with water, the filtrate acidulated with sulfuric acid until its reaction with Congo red was acid, 15 g of sodium sulfate added to the filtrate, and the solution evaporated to dryness in vacuo. The dry residue was extracted with ether for 24 hours in a Soxhlet apparatus. Driving off the ether yielded 0.8 g of an oily substance, to which 10 ml of benzene was added. The latter was evaporated to a total volume of 1-2 ml, 5 ml of ether being added to the residue and the precipitate being filtered out. Recrystallization from water yielded 0.3 g of the crystal hydrate of the diketocarboxylic acid (VI), which fused at 201-203° with decomposition.

Preparation of the p-nitrophenylhydrazone of the diketocarboxylic acid (VI). A solution of 0.65 g of p-nitrophenylhydrazine in 5 ml of 50% alcohol was added to a solution of 0.3 g of the acid in 5 ml of 50% alcohol. Two days later the reaction mixture was poured into 50 ml of water, and the resulting precipitate was filtered out. Recrystallization from 7 ml of 30% acetic acid yielded 0.2 g of a substance with a decomp. temp. of 290-292°.

Found %: C 53.35; H 4.73. $C_{13}H_{13}O_5N_3$. Calculated %: C 53.61; H 4.47.

Preparation of the p-nitrobenzyl ester of the diketocarboxylic acid (VI). 0.7 g of the acid was dissolved in 30 ml of water and accurately neutralized with a 0.1 N alkali solution, the resulting solution of the sodium salt being evaporated to a total volume of 5 ml; 1.1 g of p-nitrobenzyl bromide was heated in 10 ml of alcohol until it dissolved, and the aqueous solution of the sodium salt of the diketocarboxylic acid (VI) was added to the hot alcoholic solution. The mixture was boiled for 1 hour, a precipitate beginning to settle out after 40-45 minutes had elapsed. After the reaction mass had cooled, the precipitate was filtered out. Weight: 0.8 g. The resultant ester was recrystallized from 80% acetic acid, from which it settled out as elongated rhombohedra; m.p. 189°.

Found %: C 57.92; H 4.62. $C_{14}H_{13}O_6N$. Calculated %: C 57.73; H 4.46.

Preparation of the p-nitrophenylhydrazone of the p-nitrobenzyl ester of the diketocarboxylic acid (VI). 0.15 g of the p-nitrobenzyl ester described above was dissolved at 80° in 15 ml of glacial acetic acid; the solution was cooled to 25°, and 0.25 g of p-nitrophenylhydrazine dissolved in 10 ml of glacial acetic acid was added. Twelve hours later the reaction mixture was poured into 100 ml of water, the resulting precipitate being filtered out and washed with water. Weight: 0.25 g. The substance was recrystallized from 15 ml of glacial acetic acid and then dissolved in 3 ml of nitrobenzene heated to 80°; the resultant solution was cooled, and 10 ml of benzene was added. The resultant precipitate was filtered out 30 minutes later; it weighed 0.1 g and had a m.p. of 216-218°.

Found %: C 56.59; H 4.13; M 412 (in nitrobenzene). $C_{20}H_{18}O_7N_4$. Calculated %: C 56.34; H 4.22; M 426.

Determination of the $-CO-CH_3$ group in the molecule of the diketocarboxylic acid (VI). 0.3 g of the acid was dissolved in 10 ml of water, 1.9 g of iodine dissolved in 10 ml of a 20% aqueous solution of potassium iodide was added, and 10 ml of a 10% sodium hydroxide solution was gradually added to the resulting mixture. The solution was decolorized and iodoform gradually settled out. One hour later the latter was extracted repeatedly with ether, the ether solution being dried with sodium sulfate and the ether driven off. This yielded 0.06 g (10%) of iodoform, with a m.p. of 119°.

SUMMARY

The required conditions and the nature of the hydrolytic cleavage of 6-methyl-3-hydroxy-1,4-benzoquinone have been investigated. It has been shown that this process involves two stages: at first, the initial quinone is hydrated, and only thereafter is the ring grouping of the intermediate hydration product cleaved hydrolytically. The structure of this intermediate compound and of the final diketocarboxylic acid has been established.

Comparison of the results of these researches with the data published earlier indicates that hydrolytic ring cleavage is characteristic of all the hydroxy-1,4-quinones of benzene, naphthalene, and phenanthrene that contain a hydrogen atom or an alkyl radical at the 2 position and a hydroxyl group at the 3 position.

The mechanism of this reaction has been established experimentally.

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Received June 30, 1950

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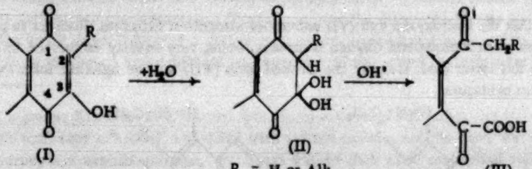
OXIDATIVE AND OXIDATIVE-HYDROLYTIC TRANSFORMATIONS OF ORGANIC MOLECULES

XXII. HYDROLYTIC AND OXIDATIVE TRANSFORMATIONS OF 1-BENZENEAZO-3,4-DIHYDROXYNAPHTHALENE[1]

O.M. Shemyakina, B.M. Bogoslovsky, and M.M Shemyakin

In several previous reports [1-4] it has been shown that the ring groups of molecules of Type (I) hydroxyquinones can be hydrated and then cleaved hydrolytically as follows:

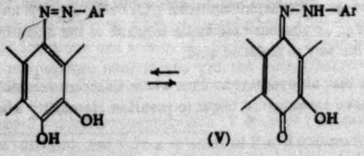


(I) (II) (III)

R = H or Alk

This reaction is easily carried out in the hydroxyquinones of the benzene, naphthalene, and phenanthrene series that contain a hydrogen atom or an alkyl radical at the 2 position, so that a tendency to such transformations may now be regarded as a characteristic feature of this group of hydroxyquinones.

It was highly probable that similar ring cleavage would take place in some hydroxyazo dyes, such as those of Type (IV), which may also exists in the tautomeric form (V) as we know:



(IV) (V)

Compounds of the latter type may be regarded as arylhydrazones of the respective hydroxyquinones, and it is that very circumstance that led us to suppose that hydroxyazo dyes of Type (IV) would behave like the Type (I) hydroxyquinones in the presence of hydrolyzing agents.

In order to make an experimental study of this problem we chose as our first research object 1-benzeneazo-3,4-dihydroxynaphthalene (VI), which ought to undergo hydrolytic cleavage very readily, for the following reasons, as we saw it. Because of its structure this hydroxyazo dye can exist in aqueous solution in the tautomeric form (VII), the phenylhydrazone of 3-hydroxy-1,4-naphthoquinone (especially at values of pH in excess of 7). The 3-hydroxy-1,4-naphthoquinone itself, as has been shown previously [2], is readily cleaved to o-acetylphenylglyoxylic acid in accordance with the general reaction set forth above, (I) → (II) → (III), when it is boiled in an aqueous solution (pH = 7.3-9.5). We therefore thought that the tautomeric form (VII) of the initial hydroxyazo dye ought to be just as readily cleaved between the 2 and 3 carbon atoms, either before or after the phenylhydrazine group at the 1 position was split off.

An experimental study of the conditions and nature of the hydrolytic cleavage of the hydroxyazo dye (VI) we had chosen showed that this assumption was correct. This hydroxyazo dye begins to undergo a slow change when an aqueous solution that has an initial pH of 7 is boiled, provided atmospheric oxygen is excluded (nitrogen atmosphere). These changes occur very rapidly when the solution pH is 9, being fully completed within 15 hours of boiling when that is so. We found that it is the quinoid form (VII) of the azo dye rather than the benzoid form (VI) that is cleaved hydrolytically, the (VII) form splitting off the phenylhydrazine group and being converted into 3-hydroxy-1,4-naphthoquinone (VIII), secured in yields as high as 50%, which then undergoes more far-reaching changes, being partially cleaved to o-acetylphenylglyoxylic acid (X): we isolated a small amount of this latter acid as the corresponding semicarbazone.

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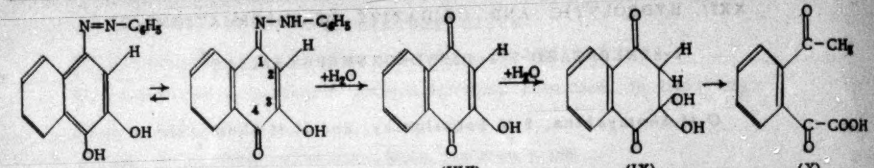
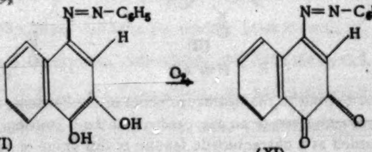
[1] Communication XIV on the hydrolytic cleavage of carbon bonds.



(VI) (VII) (VIII) (IX) (X)

Thus, the phenylazo group can be split out of the 1-benzeneazo-3,4-dihydroxynaphthalene molecule (VI) and one of the naphthalene rings can then be cleaved by the action of hydrolyzing agents alone, the required conditions being fairly mild.

It should be stressed that the hydroxyazo dye (VI) undergoes altogether different changes in aqueous or aqueous–alcoholic alkali solutions when atmospheric oxygen is present, being very readily converted into 1-benzeneazo-3,4-naphthoquinone (XI); in this latter case, it is not the quinoid form (VII) but the benzoid form (VI) of the initial hydroxyazo dye that undergoes oxidation.



(VI) (XI)

This process, first described by Zincke and Wiegand [5], has also been explored by us. We have found that oxidation of the hydroxyazo dye (VI) by oxygen in an aqueous–alcoholic alkali solution is completed within 2-2.5 hours at 5-10°, the yield of 1-benzeneazo-3,4-naphthoquinone (XI) being 65-70% under these conditions.* The ring of this azoquinone is unstable; heating an aqueous–alcoholic solution of the azoquinone to about 180° in nitrogen results in cleaving its molecule all the way to phthalic acid.

In conclusion, we might add that all hydroxyazo dyes whose structure resembles that of the 1-benzeneazo-3,4-dihydroxynaphthalene (VI) we have investigated ought to manifest instability when acted upon by oxidants and hydrolyzing agents.

EXPERIMENTAL

1. Hydrolytic cleavage of 1-benzeneazo-3,4-dihydroxynaphthalene. The experiment was performed in apparatus consisting of two 3-liter round-bottomed flasks. The first flask (A) was fitted with a reflux condenser and two tubes extending to the bottom of the flask. The other flask (B) was fitted with a reflux condenser, a dropping funnel, and one tube extending to the bottom of the flask. The two flasks were connected via a three-way stopcock, to which there were attached: one of the tubes in the flask (A), the upper end of the condenser fitted to flask (A), and the tube in flask (B). Nitrogen was supplied to the system through the other tube in flask (A), the nitrogen being purified by first passing it through an alkaline solution of pyrogallol and conc.sulfuric acid. The nitrogen had to pass through a tube filled with copper and heated to 400-450° to get rid of the last traces of oxygen. The system terminated in two Tishchenko bottles filled with an alkaline solution of pyrogallol, which were connected to the upper end of the condenser on tube (B).

3 g of 1-benzeneazo-3,4-dihydroxynaphthalene [5] was placed in flask (B), and 2 liters of a phosphate buffer solution (pH 9.17; buffer capacity 0.1 mole) in flask (A). The airtightness of the system was checked, and then we began to drive the air out of the system by nitrogen, the three-way stopcock being turned so as to connect the upper end of the condenser on flask (A) to the tube that reached to the bottom of flask (B).

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* Zincke and Wiegand give 250° as the decomposition temperature of this azoquinone, whereas it actually fuses with decomposition at 205-207°.

At the same time the phosphate buffer solution in flask (A) was heated until it boiled. Two hours after the solution had started to boil, the three-way stopcock was turned so as to cover up the opening leading to the condenser of flask(A), and the air was driven out of the flask (A) tube by the buffer solution, without stopping the flow of nitrogen, the buffer solution rising up to the three-way stopcock. The three-way stopcock was then turned to its initial position and nitrogen was passed through for another 0.5 hour. Then the heating of flask (A) was stopped, the buffer solution was cooled, and the three-way stopcock was turned so as to connect the tube in flask (A) to the tube in flask (B), after which the buffer solution was transferred to flask (B), which contained the sample of the substance.

The resultant mixture was boiled in a current of nitrogen for 15 hours. After heating was complete, the reaction mixture was cooled, the solution pH was brought to 6-6.5 by adding 25% sulfuric acid, and the solution was then evaporated in vacuo in a current of nitrogen until its volume totaled some 200 ml. When it had cooled, the dark-brown precipitate was filtered out, and the brown-red filtrate was acidulated with 60% sulfuric acid. This threw down 0.78 g of a yellow precipitate, which had a m.p. of 190-191° after double recrystallization from methanol and exhibited no depression of the mixed melting point with 3-hydroxy-1,4-naphthoquinone.

The acid aqueous filtrate was extracted five times with ether, the ether extract was washed with water, boiled with activated charcoal, and dried with sodium sulfate, and the ether was driven off. This left 0.2 g of 3-hydroxy-1,4-naphthoquinone, which was washed with small portions of ether and ethyl alcohol and then recrystallized from methanol. M.p. 190-191°. The total yield of the 3-hydroxy-1,4-naphthoquinone was 49.5%.

The aqueous reaction solution left after the hydroxyquinone had been extracted with ether was evaporated in vacuo to a volume of 30-40 ml, the mineral salts being filtered out and the filtrate extracted with ether. The ether extract was boiled with activated charcoal, the ether driven off, and the yellow oily residue was dissolved in 2 ml of ethyl alcohol, after which a solution of 0.1 g of semicarbazide hydrochloride and 0.14 g of sodium acetate in 1 ml of water was added. A few days later 0.02 g of a precipitate that had a m.p. of 154-156° with decomposition settled out of the solution. After crystallization from water containing activated charcoal the substance had a m.p. of 158-160° with decomposition and exhibited no depression of the decomposition temperature when mixed with the semicarbazone of o-acetylphenylglyoxylic acid [2].

2. Oxidizing 1-benzeneazo-3,4-dihydroxynaphthalene. 1 gram of 1-benzeneazo-3,4-dihydroxynaphthalene was mixed with 25 ml of alcohol, and then a solution of 2 g of sodium hydroxide in 10 ml of water was added. Oxygen was passed through the resultant dark-blue solution, chilled to 5-10°, for 2-2.5 hours until the solution turned brown.[*]

Within 30-45 minutes a light-yellow precipitate began to settle out of the solution, its amount gradually increasing. When the reaction was over, the precipitate was filtered out, thoroughly mixed with 10-15 ml of water, refiltered, repeatedly washed on the filter with water. Weight: 0.70 g; 70% yield.

The synthesized 1-benzeneazo-3,4-naphthoquinone was purified by extracting it with ether in a device used for hot extraction. Light-yellow crystals that fused at 205-207° with decomposition settled out of the ether solution.

Found %: C 73.34; H 4.12. $C_{16}H_{10}O_2N_2$. Calculated %: C 73.28; H 3.84.

3. Cleaving 1-benzeneazo-3,4-naphthoquinone. 1 g of 1-benzeneazo-3,4-naphthoquinone was heated for 6 hours to 200° (bath temperature) with 30 ml of 20% aqueous alcohol in an autoclave (from which the air had previously been expelled by nitrogen). When the reaction was over, the black precipitate was filtered out, the filtrate being alkalinized and repeatedly extracted with ether. Then the aqueous-alkaline solution was acidulated with hydrochloric acid and evaporated to dryness. The residue was extracted with ether in a Soxhlet apparatus, the resulting ether solution boiled with activated charcoal and dried with

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[*] Oxidation may also be effected with atmospheric oxygen, but then the reaction is slower.

sodium sulfate, and the ether driven off. The residual crystalline precipitate was washed with a few drops of ether and recrystallized from water. The substance fused with decomposition at 195-200° and exhibited no depression of the decomposition temperature when mixed with phthalic acid; it was converted to phthalic anhydride (m.p. 130-131°) by heating it above the decomposition temperature.

SUMMARY

It has been shown that 1-benzenazo-3,4-dihydroxynaphthalene is changed very readily when acted upon by oxidants or hydrolyzing agents. This hydroxyazo dye is readily oxidized in an aqueous-alcoholic alkaline solution to 1-benzeneazo-3,4-naphthoquinone by atmospheric oxygen at 5-10°, while in the absence of atmospheric oxygen it undergoes profound hydrolytic transformations when an aqueous solution with a pH of 9 is boiled. In the latter case, the 1-benzeneazo-3,4-dihydroxynaphthalene is first converted into the tautomeric quinoid form (the phenylhydrazone of 3-hydroxy-1,4-naphthoquinone), which splits off the phenylhydrazine group to yield 3-hydroxy-1,4-naphthoquinone, which is then partially cleaved to o-acetylphenylglyoxylic acid.

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Received June 30, 1950

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OXIDATIVE AND OXIDATIVE-HYDROLYTIC TRANSFORMATIONS OF ORGANIC MOLECULES

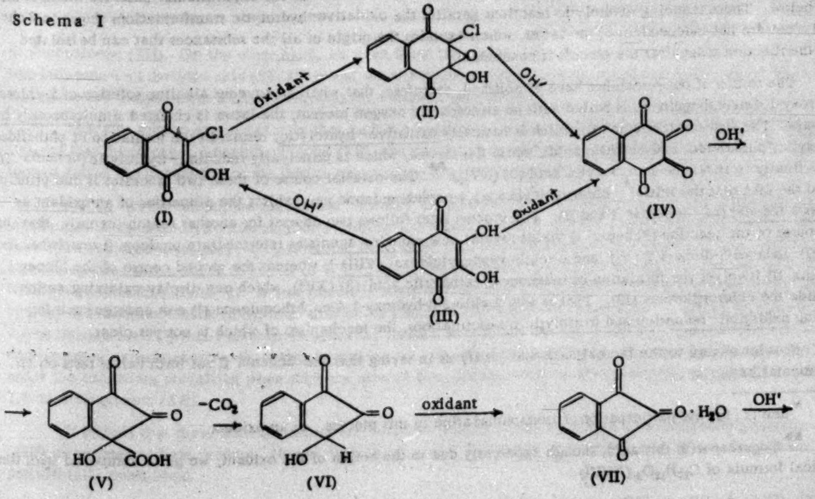
XXIII. The Mechanism Involved in Oxidation-Reduction and Hydrolytic Transformations of 2-Chlorohydroxy-1,4-Naphthoquinone

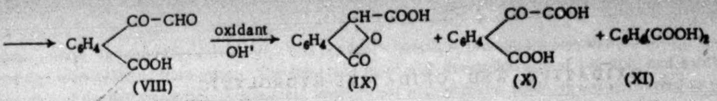
D.P.Vitkovsky and M.M.Shemyakin

We recently showed [1] that when an aqueous alkaline solution of 2-chloro-3-hydroxy-1,4-naphthoquinone (I) is boiled in the absence of atmospheric oxygen, it gradually undergoes profound changes, finally yielding the following compounds: phthalidecarboxylic acid (14%), phthalonic acid (2%), phthalic acid (1%), indanone-1-carboxylic acid-(3) (18%), and 2,3-dihydroxy-1,4-naphthoquinone (56%). We have now discovered another product of the conversion of 2-chloro-3-hydroxy-1,4-naphthoquinone: a red crystalline substance with a m.p. of 315°, the elementary composition of which is given by the empirical formula $C_{27}H_{12}O_3$. When this reaction is carried out with atmospheric oxygen present, the end products comprise only the following of the compounds enumerated above [1]: phthalidecarboxylic acid (52%), phthalonic acid (11%), and phthalic acid (13%).

As for the way in which 2-chloro-3-hydroxy-1,4-naphthoquinone is converted into these three acids, we have already dealt with this problem in one of our preceding reports [1]; it was found that the mechanism involved in the production of these acids is the same whether atmospheric oxygen is present or not. Their formation stems from the fact that 2-chloro-3-hydroxy-1,4-naphthoquinone (I) can be oxidized to 1,2,3,4-tetraoxotetralin (IV) (more precisely, its hydrate) either via the corresponding oxide (II) or via 2,3-dihydroxy-1,4-naphthoquinone (isonaphthazarine) (III), the compound (IV) being converted by the alternating action of oxidizing and hydrolyzing agents, via a series of intermediate steps, into phthalidecarboxylic, phthalonic, and phthalic acids, in accordance with the schema set forth below (see [1,2] for details).

Schema I




(VIII) (IX) (X) (XI)

As we see in Schema I, the formation of the end-product acids from 2-chloro-3-hydroxy-1,4-naphthoquinone entails the necessary participation of an oxidizing agent in three of the intermediate stages of the transformations in question. Whenever the reaction is carried out in the presence of atmospheric oxygen, the latter assumes the role of the oxidant. But the problem of which compound or compounds act as oxidants when the reaction is carried out with atmospheric oxygen excluded (in an atmosphere of nitrogen) has remained moot up to the present time, making it impossible to render a final judgment concerning the nature of the complicated chain of reactions that results in the formation of the substances enumerated above. Inasmuch as a solution of this problem was of interest in comprehending the nature of the oxidative-hydrolytic transformations of carbocyclic compounds, we have devoted the present paper to its elucidation.

We must begin by emphasizing that though nothing but phthalidecarboxylic, phthalonic, and phthalic acids are produced when the process is carried out with atmospheric oxygen present, isonaphthazarine (III), indanone-1-carboxylic acid-(3) (XVII) and a substance with the empirical formula of $C_{27}H_{12}O_3$ (XVIII) are also produced when atmospheric oxygen is excluded. It is sufficiently obvious that the isonaphthazarine arises as the result of the direct substitution of a hydroxyl group for the chlorine atom in the 2-chloro-3-hydroxy-1,4-naphthoquinone molecule under the action of the aqueous alkali solution. Inasmuch as isonaphthazarine is highly stable when no atmospheric oxygen is present [2], it is evident that it is accumulated in very large quantities under these circumstances. Isonaphthazarine can also be produced as an intermediate compound when the reaction is carried out with atmospheric oxygen present, but under these conditions it is converted at a high rate into phthalidecarboxylic, phthalonic, and phthalic acid [2], which explains why it cannot be found among the reaction products in this case as a rule.

We have now established that the following compounds: the initial 2-chloro-3-hydroxy-1,4-naphthoquinone [or more correctly, its tautomeric form (IB)] and the intermediate indenone-1-carboxylic acid (XVI), whose reduction product is the indanone-1-carboxylic acid (XVII) large quantities of which are usually secured, act as oxidants[*] in the oxidative-hydrolytic transformations represented in Schema I when no atmospheric oxygen is present.

The 2-chloro-3-hydroxy-1,4-naphthoquinone (I) is converted into the terminal acid (XVII) as the result of a series of reducing-hydrolytic and other reactions, represented in Schema II, the experimental basis for which is set forth below. These reducing—hydrolytic reactions parallel the oxidative—hydrolytic transformations shown in Schema I, but are not independent of the latter, which explains the origin of all the substances that can be isolated from the reaction mass after the process is concluded.

The results of our researches have established, therefore, that when an aqueous alkaline solution of 2-chloro-3-hydroxy-1,4-naphthoquinone is boiled with no atmospheric oxygen present, the latter is changed simultaneously in two ways. The first one (Schema I), which is basically oxidative—hydrolytic, results in the formation of phthalidecarboxylic, phthalonic, and phthalic acids, while the second, which is principally reducing—hydrolytic (Schema II) results finally in indanone-1-carboxylic acid-(3) (XVII).[**] The parallel course of these two processes is due principally to the fact that the initial 2-chloro-3-hydroxy-1,4-naphthoquinone can exhibit the properties of an oxidant as well as a reducer (cf. Schemas I and II). The process later follows two courses for another reason, namely, that the first course of the reaction (Schema I) yields several new reducing agents as intermediate products [isonaphthazarine (III), indanol-3-dione-1,2 (VI), and o-carboxyphenylglyoxal (VIII)], whereas the second course of the process (Schema II) involves the formation of indenone-1-carboxylic acid-(3) (XVI), which can display oxidizing action alongside the chlorotriketone (IB). That is why 2-chloro-3-hydroxy-1,4-naphthoquinone (I) can undergo such far-reaching oxidation—reduction and hydrolytic transformations, the mechanism of which is not yet clear.

Now let us turn to the factual data that justify us in saying that the Schema II set forth below rests on an experimental basis.

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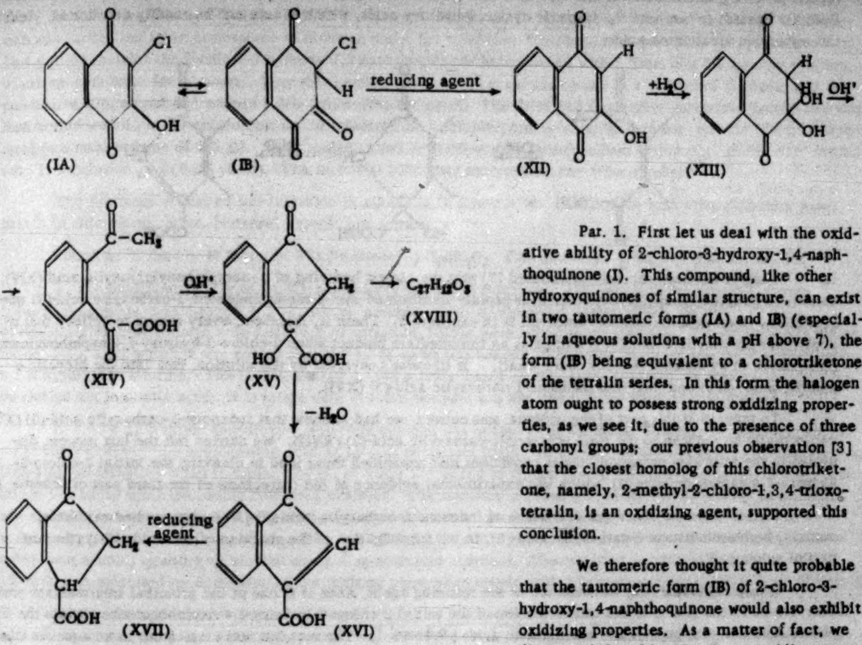
[*] See [1] for the participation of isonaphthazarine in this process as an oxidant.

[**] Together with this acid, though apparently due to the action of the oxidant, we get a compound with the empirical formula of $C_{27}H_{12}O_3$ (XVIII).

Schema II



Par. 1. First let us deal with the oxidative ability of 2-chloro-3-hydroxy-1,4-naphthoquinone (I). This compound, like other hydroxyquinones of similar structure, can exist in two tautomeric forms (IA) and IB) (especially in aqueous solutions with a pH above 7), the form (IB) being equivalent to a chlorotriketone of the tetralin series. In this form the halogen atom ought to possess strong oxidizing properties, as we see it, due to the presence of three carbonyl groups; our previous observation [3] that the closest homolog of this chlorotriketone, namely, 2-methyl-2-chloro-1,3,4-trioxotetralin, is an oxidizing agent, supported this conclusion.

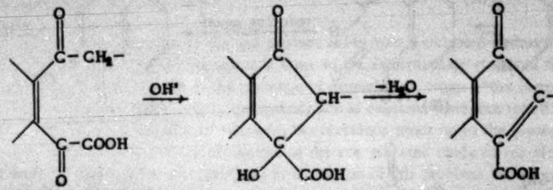
We therefore thought it quite probable that the tautomeric form (IB) of 2-chloro-3-hydroxy-1,4-naphthoquinone would also exhibit oxidizing properties. As a matter of fact, we discovered that this quinone can oxidize monovalent negative iodine to free iodine, for example, being itself reduced to 3-hydroxy-1,4-naphthoquinone (XII). On the other hand, we have found that 3-hydroxy-1,4-naphthoquinone (XII) can be converted into indanone-1-carboxylic acid-(3) (XVII) and the compound $C_{27}H_{12}O_3$ (XVIII) under the conditions in which these substances are formed from 2-chloro-3-hydroxy-1,4-naphthoquinone (I).

This also proved experimentally that 2-chloro-3-hydroxy-1,4-naphthoquinone (I) possesses oxidizing properties and that 3-hydroxy-1,4-naphthoquinone (XII), the product of its reduction, is the first intermediate substance formed during the conversion of the initial quinone into the final compounds.

Par. 2. As for the second part of the Schema in question (XII) → (XIII) → (XIV), the feasibility and the mechanism of the hydrolytic cleavage of 3-hydroxy-1,4-naphthoquinone (XII) to o-acetylphenylglyoxylic acid (XIV) have been explored previously [4,5], it having been found that this reaction can be carried out with ease in a boiling aqueous solution whose pH is in excess of 7, i.e., under the conditions prevailing during the cleavage of 2-chloro-3-hydroxy-1,4-naphthoquinone (I). It was therefore fairly obvious that o-acetylphenylglyoxylic acid (XIV), like 3-hydroxy-1,4-naphthoquinone (XII), must also be an intermediate product in the transformation of 2-chloro-3-hydroxy-1,4-naphthoquinone (I) into indanone-1-carboxylic acid-(3) (XVII) and the compound $C_{27}H_{12}O_3$ (XVIII). As we have demonstrated experimentally, these two substances are actually produced from o-acetylphenylglyoxylic acid (XIV) under the conditions prevailing when they are secured from 2-chloro-3-hydroxy-1,4-naphthoquinone (I) and 3-hydroxy-1,4-naphthoquinone (XII).

It follows that these transformations are doubtless related to the formation of acetylphenylglyoxylic acid (XIV) as an intermediate product. Hence, both the first and the second parts of Schema II may be regarded as experimentally established.

Par. 3. Now let us turn to consideration of the third part of this schema (XIV) → (XV) → (XVI), dealing with the further changes in o-acetylphenylglyoxylic acid (XIV). As has been noted more than once in our previous reports [2,4,6-9], diketo acids of this type exhibit a great tendency (particularly when their aqueous—alkaline solutions are heated) to turn into the isomeric cyclic α-hydroxy acids, which in turn can be readily dehydrated, yielding the respective unsaturated acids:



Thus, it has been recently established [7] that the closest homolog of o-acetylphenylglyoxylic acid (XIV), namely, o-propionylphenylglyoxylic acid, is rapidly transformed into 2-methylindenone-1-carboxylic acid-(3) when it is boiled in an aqueous solution whose pH is in excess of 7. There is, therefore, every reason to believe that o-acetylphenylglyoxylic acid (XIV), formed as an intermediate product when 2-chloro-3-hydroxy-1,4-naphthoquinone (I) is boiled in an aqueous solution of an alkali, is likewise converted by the solution, first into the bicyclic α-hydroxy acid (XV) and then into indenone-1-carboxylic acid-(3) (XVI).*

To prove that this part of the schema was correct, we had to show that indenone-1-carboxylic acid-(3) (XVI) can actually be reduced to the final indanone-1-carboxylic acid-(3) (XVII). We carried out the last process, discussed in the following paragraph, under conditions that resembled those used in cleaving the initial 2-chloro-3-hydroxy-1,4-naphthoquinone (I), which was experimental evidence of the correctness of the third part of Schema II.

Par. 4. We used a halogen derivative of indenone-1-carboxylic acid-(3) (XVI) that we had available, namely, 2-chloroindenone-1-carboxylic acid-(3), in our investigation of the reaction of the acid (XVI) (the last part of Schema II).

Isonaphthazarine (III) was selected as the reducing agent, since it is one of the principal intermediate products formed in the course of the transformation of the initial 2-chloro-3-hydroxy-1,4-naphthoquinone (I) into the final phthalidecarboxylic, phthalonic, and phthalic acids (Schema I). The reaction was carried out in an aqueous alkaline solution in an atmosphere of nitrogen, complying with all the conditions required for the formation of these three acids and indanone-1-carboxylic acid-(3) (XVII) from the 2-chloro-3-hydroxy-1,4-naphthoquinone (I). As we expected, we found all the four acids specified above in the reaction solution after the process was complete, whereas the 2-chloroindenone-1-carboxylic acid-(3) yielded no indanone-1-carboxylic acid-(3) (XVII) in a blank test, run without any isonaphthazarine.

Hence, indenone-1-carboxylic acid-(3) (XVI) is actually a predecessor of the final indanone-1-carboxylic acid-(3) (XVII). The latter is produced by the hydrogenation of the indenone-1-carboxylic acid-(3) (XVI) by isonaphthazarine (III) and, evidently, by the other reducing agents [Compounds (VI) and (VIII)] formed during the oxidative—hydrolytic transformation of the initial 2-chloro-3-hydroxy-1,4-naphthoquinone (I) into phthalidecarboxylic, phthalonic, and phthalic acids (see Schemas I and II).

We may thus consider that all the stages of the mechanism we have advanced for the oxidation—reduction and hydrolytic transformations of 2-chloro-3-hydroxy-1,4-naphthoquinone, illustrated in Schemas I and II, have been proved.

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* Apparently the bicyclic α-hydroxy acid (XV) is the ancestor of the substance with the empirical formula of $C_{27}H_{12}O_3$, as well as of the unsaturated acid (XVI). This compound (XVIII) is probably formed by the condensation of three molecules of the α-hydroxy acid (XV), while it is oxidatively decarboxylated at the same time, as is often the case, we know, in cyclic α-hydroxy acids of this sort (cf. [4]):

$$\underset{(XV)}{3C_{10}H_8O_4} = \underset{(XVIII)}{C_{27}H_{12}O_3} + 3CO_2 + 3H_2O + 6H.$$

In this process the dehydrogenating action is evidently due to the tautomeric form of the initial quinone (IB) and the unsaturated acid (XVI), which is reduced to indanone-1-carboxylic acid-(3) (XVII). The question of the structure of the substance (XVIII) is still unsolved.

EXPERIMENTAL[*]

1. Transformations of 2-chloro-3-hydroxy-1,4-naphthoquinone in an aqueous solution of an alkali. The reaction was carried out in an atmosphere of nitrogen under the conditions stipulated in Report XXII [10] (experiment 1), 10.4 g (0.05 mole) of the 2-chloro-3-hydroxy-1,4-naphthoquinone being boiled with 5 liters of a 1% aqueous solution of sodium hydroxide for 24 hours. After this heating the reaction mass was cooled in a current of nitrogen, and the precipitate filtered out and washed a few times with hot water. The dried and thoroughly pulverized precipitate was then boiled with 50 ml of chloroform for 30 minutes, the insoluble portion being filtered out, and the filtrate evaporated to a total volume of 2-3 ml. As it cooled, a red crystalline substance (needles) with a m.p. of 309-310° settled out. It weighed 0.06 g (0.9% yield). The m.p. was 315° after recrystallization from alcohol.[**]

The substance produced was insoluble in alkalis or in dilute acids; it dissolved with some difficulty when heated in chloroform, ether, benzene, xylene, and tetralin.

Found %: C 84.49; H 3.49; M 373 (in phenol). $C_{27}H_{12}O_3$. Calculated %: C 84.37; H 3.13; M 384.

2. The oxidizing ability of 2-chloro-3-hydroxy-1,4-naphthoquinone. a) 0.1417 g of 2-chloro-3-hydroxy-1,4-naphthoquinone was heated in 30 ml of alcohol until it dissolved, after which 30 ml of concentrated hydrochloric acid and 2.0 g of potassium iodide were added to the solution. The mixture was boiled for 45 min, after which it was cooled and 250 ml of water was added. The iodine liberated was titrated back with 0.1 N hyposulfite solution. The iodine totaled 0.1588 g (92%, based on the initial quinone). A similar reaction can be carried out in acetic acid; it is rather slow at room temperature and much faster when heat is applied.

b) 0.50 g of 2-chloro-3-hydroxy-1,4-naphthoquinone was heated in 40 ml of alcohol until it dissolved, and 50 ml of concentrated hydrochloric acid and 3 g of potassium iodide were added to the solution. The mixture was boiled for 45 minutes; when it cooled 200 ml of water was added to it, and then a 5% aqueous solution of sodium bisulfite was added until the iodine color had vanished. The resultant solution was extracted repeatedly with ether, and the ether extract was washed with a concentrated solution of potassium chloride and then with water and dried with calcium chloride. Driving off the ether left behind 0.40 g of a crystalline substance, which was recrystallized twice from a small quantity of alcohol containing activated charcoal. The resultant compound had a m.p. of 190-191° and exhibited no depression of the melting point when mixed with 3-hydroxy-1,4-naphthoquinone. 97% yield.

3. Transformations of 3-hydroxy-1,4-naphthoquinone in an aqueous solution of an alkali. The reaction was carried out in an atmosphere of nitrogen, under the conditions set forth in Report XXII [10] (Experiment 1), 10.44 g (0.06 mole) of 3-hydroxy-1,4-naphthoquinone being boiled for 24 hours with 6 liters of a 1% aqueous solution of sodium hydroxide. Soon after boiling began, a precipitate began to settle out of the reaction solution, its quantity gradually increasing. When heating was over, the reaction mixture was cooled in a current of nitrogen, after which the resultant precipitate was filtered out and washed a few times with hot water. It weighed 2.3 g; the m.p. was 345-370° (the analysis of this substance is described below).

The pH of the solution was brought down to 6.5-7.0 by adding sulfuric acid, and then the solution was evaporated in a current of nitrogen until its volume totaled 400-500 ml. The precipitated silicic acid[***] was filtered out, boiled with 20 ml of water, and refiltered, this operation being repeated two more times. The wash waters were combined with the bulk of the filtrate, and conc. sulfuric acid was added until it constituted 10% of the solution; during acidulation an emulsion settled out at first, followed by the formation of a highly tarred precipitate, which was filtered out and washed with water. The filtrate was decolorized with activated charcoal and then extracted 5 times with chloroform. The extract was dried with calcium chloride and filtered, after which the solvent was driven off. This yielded 3.2 g of a dark, noncrystallizing oil, which was heated in 100 ml of water until it dissolved and then boiled with activated charcoal for 10 minutes, after which the charcoal was filtered out. As it cooled, a crystalline precipitate settled out, which was filtered out and air-dried the next day.

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[*] The analytical portion of this research was carried out with the participation of E.A.Ignatyeva, to whom we are deeply grateful.

[**] The analysis of the reaction solution is described in Report XVII [1].

[***] The silicic acid was produced during the reaction by the action of the alkali solution upon the surface of the glass flask.

It weighed 3.0 g; its m.p. was 81-82°. The m.p. of the substance was raised to 83-84° after recrystallization from water; its mixed melting point with the indanone-1-carboxylic acid-(3) described previously [1] exhibited no depression. Evaporating the aqueous mother liquor yielded a little more of this acid. The acid yield was 29%. No phthalidecarboxylic, phthalonic, or phthalic acid was found in the reaction products.

The substance with a m.p. of 345-370° described above, which was recovered at the end of the reaction, was dissolved in 1.5 liters of boiling chloroform. The solution was evaporated to a volume of about 100 ml, and the resulting precipitate was filtered out. This yielded 0.9 g of a substance as elongated yellow filaments with a m.p. of 371° (this substance was not investigated further). The filtrate was concentrated to a volume of some 50 ml; after it had stood for a long time, orange-red crystals began to settle out (they weighed 3.1 g; m.p. 301-310°). These crystals were recrystallized three times from xylene, twice from tetralin, and once from chloroform, after which their melting point was 315°, the mixed melting point with the compound $C_{27}H_{12}O_3$ secured in Experiment 1 exhibiting no depression.

4. Transformations of o-acetylphenylglyoxylic acid in an aqueous solution of an alkali. The reaction was carried out in an atmosphere of nitrogen under the conditions set forth in Report XXII [10] (Experiment 1), 1.9 g (0.01 mole) of o-acetylphenylglyoxylic acid being boiled for 24 hours with 1 liter of a 1% aqueous solution of sodium hydroxide. The solution, which was colorless at first, soon turned yellow, and then a yellow precipitate began to settle out, constantly increasing in size. After three to four hours had elapsed, the solution turned green. After heating was complete, the reaction mixture was cooled in a current of nitrogen, the precipitate being filtered out and washed a few times on the filter with hot water. It weighed 0.44 g; m.p. 345-370°. The precipitate was dissolved in boiling chloroform, and then the procedure described in Experiment 2 was employed to recover 0.2 g of a yellow substance with a m.p. of 371° and 0.24 g of a red substance with a m.p. of 315° from it. The latter substance was identical with the $C_{27}H_{12}O_3$ compound secured in Experiments 1 and 3.

After the precipitate had been filtered out, sulfuric acid was added to the aqueous reaction solution (until the solution pH was 6.5-7.0), and the latter was evaporated to a volume of about 150 ml and cooled, the precipitated silicic acid being filtered out. The precipitate was washed three times on the filter with small portions of hot water. The wash waters were combined with the bulk of the filtrate, and 20 ml of conc. sulfuric acid was added, throwing down a brown, tarry substance, which was filtered out. The transparent, nearly colorless filtrate was extracted with chloroform, the extract being dried with calcium chloride, and the chloroform driven off. This left 0.7 g of a yellowish oil, which was dissolved in hot water; the solution was boiled for a few minutes with activated charcoal, filtered, and cooled. 0.6 gram of indanone-1-carboxylic acid-(3) with a m.p. of 83-84° was recovered, its yield being 34%. No phthalidecarboxylic, phthalonic, or phthalic acid was found in the reaction products.

5. Reaction of 2-chloroindenone-1-carboxylic acid-(3) with isonaphthazarin. The reaction was carried out in an atmosphere of nitrogen under the conditions described in Report XXII [10] (Experiment 1), a mixture of 10.5 g (0.05 mole) of 2-chloroindenone-1-carboxylic acid-(3) and 1.90 g (0.01 mole) of isonaphthazarin being boiled for 24 hours with 0.5 liter of a 2% aqueous solution of sodium hydroxide. The solution, which was blue at first, soon turned brown, and after a few hours had elapsed, a tarry precipitate began to settle out. After heating was over, the reaction mass was cooled in a current of nitrogen and acidulated with sulfuric acid until its reaction was acid with Congo red, a large quantity of heavily tarred substances settling out. These were filtered out, and the filtrate was repeatedly extracted, first with chloroform and then with ether. The chloroform solution was dried with calcium chloride, and then the solvent was driven off until the volume of the residue totaled 2-3 ml. A very small quantity of phthalidecarboxylic acid, m.p. 151-152° (from water), gradually settled out of the solution. The chloroform mother liquor left after this acid had been filtered out was evaporated to dryness. This left a noncrystallizing oil, which was dissolved in 50 ml of hot water and boiled for a few minutes with activated charcoal, after which the charcoal was filtered out. As the solution cooled, 0.4 g of indanone-1-carboxylic acid-(3) settled out; its m.p. was 83-84° after two recrystallizations from water.

The ether solution secured earlier was evaporated, the residual oil being boiled with 20 ml of water containing activated charcoal, after which the aqueous solution was filtered and extracted with ether. Driving off the ether left an oily substance that gradually crystallized. It was recrystallized twice from water containing activated charcoal. The 0.1 g of phthalic acid recovered had a m.p. of 195-200° with decomposition; heating it above the decomposition temperature converted it into phthalic anhydride with a m.p. of

130°. An extremely small quantity of phthalonic acid, as the corresponding quinoxaline derivative with a m.p. of 237-239° (from alcohol), could be recovered by the method described previously [11] from the aqueous mother liquor left after the recrystallization of the phthalic acid.

SUMMARY

The mechanism of the oxidation-reduction and hydrolytic transformations of 2-chloro-3-hydroxy-1,4-naphthoquinone that take place when it is boiled in an aqueous alkali solution with atmospheric oxygen excluded has been investigated and established experimentally.

It has been found that the phthalidecarboxylic acid, phthalonic acid, phthalic acid, indanone-1-carboxylic acid-(3), isonaphthazarine, and the substance with the empirical formula of $C_{27}H_{12}O_3$ produced under these conditions arise as the result of two parallel interrelated processes, one of which is primarily oxidative-hydrolytic, while the other is reducing-hydrolytic. This complicated chain of transformations ends up in the formation of the end products enumerated above, recovered at the end of the process.

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Received June 30, 1951

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[7] " " " " " p. 607.

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XXXVII. THE CONVERSION OF TETRAHYDROFURFURYL ALCOHOL AND TETRAHYDROFURFURYLTHIOL INTO Δ^2-DIHYDROTHIOPYRAN

Yu. K. Yuryev and E. G. Vendelshtein

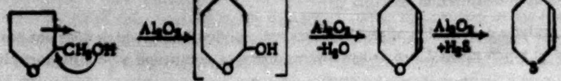
In previous papers one of the present authors has shown that furanidine (tetrahydrofuran) and its homologs are converted into thiophane and the latter's respective homologs [1] by the action of hydrogen sulfide at 250-400° over alumina and that Δ^2-dihydropyran and tetrahydropyran undergo a similar transformation, yielding Δ^2-dihydrothiopyran [2] and tetrahydrothiopyran [3], respectively.

In the present research we have explored the behavior of tetrahydrofurfuryl alcohol in this reaction, and the behavior of tetrahydrofurfurylthiol when in contact with alumina.

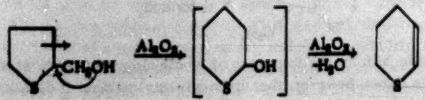
Dehydrating tetrahydrofurfuryl alcohol at 300-375° over alumina involves the conversion of the five-membered oxygen-containing ring into a six-membered ring, resulting in the formation of Δ^2-dihydropyran [4]. We therefore expected that reacting tetrahydrofurfuryl alcohol with hydrogen sulfide over alumina would yield Δ^2-dihydrothiopyran, both as the result of the conversion of Δ^2-dihydropyran (Schema I) and, possibly, as the result of dehydration coupled with expansion of the ring of the intermediate α-hydroxymethylthiophane (Schema II). Inasmuch as thiols are produced by the combined catalytic dehydration of alcohols and hydrogen sulfide at 300-380°, it was quite possible that tetrahydrofurfurylthiol and α-mercaptomethylthiophane would be produced as intermediates when tetrahydrofurfuryl alcohol was reacted with hydrogen sulfide.

We found earlier that functional derivatives of the furan and furanidine series (alcohols, aldehydes, and ketones [6], and acid esters [7]) are unstable during the catalytic conversion of heterocyclic compounds. We believe that α-hydroxymethylthiophane (Schema II), tetrahydrofurfurylthiol (Schema III), and α-mercaptomethylthiophane (Schema IV) should undergo isomerization, like tetrahydrofurfuryl alcohol (Schema I), when placed in contact with alumina at high temperatures (300-350°), being converted into six-membered heterocyclic compounds with the same hetero atoms and with a hydroxyl or a sulfhydryl group attached to the alpha carbon atom of the ring. Subsequent splitting off of water or hydrogen sulfide from these compounds ought to yield Δ^2-dihydrothiopyran (Schemas II and IV), Δ^2-dihydropyran (Schemas I and III), respectively, the Δ^2-dihydropyran being converted into Δ^2-dihydrothiopyran (Schemas I and III) by its reaction with hydrogen sulfide (either introduced into the reaction or produced therein):

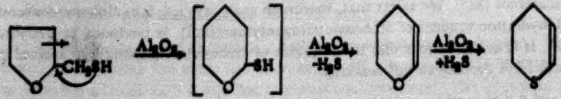
(I)



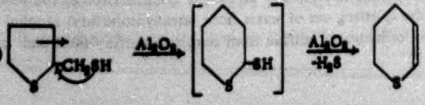
(II)



(III)



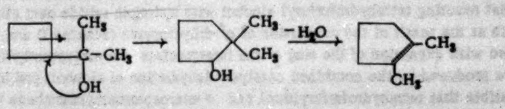
(IV)



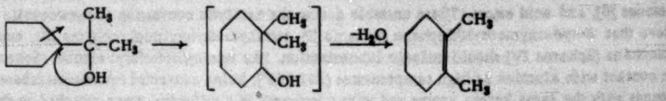
It is highly probable that the reaction can follow the course of Schema III, i.e., with tetrafurfuryl alcohol first giving rise to tetrahydrofurfurylthiol, since we secured Δ^2-dihydrothiopyran by placing tetrahydrofurfurylthiol in contact with alumina at 300° (the reaction was accompanied by the evolution of hydrogen sulfide). Thus, the synthesis of Δ^2-dihydrothiopyran from tetrahydrofurfurylthiol (Schema III) – the conversion of a five-membered oxygen-containing heterocyclic compound into a six-membered sulfur-containing one – seemed to us to be a three-stage process, like the synthesis of Δ^2-dihydropyran from tetrahydrofurfuryl alcohol followed by its conversion into Δ^2-dihydrothiopyran (Schema I).

We believe that the cited schemas of the mechanism involved in the conversion of functional derivatives of saturated five-membered heterocyclic compounds into unsaturated six-membered ones containing the same hetero atoms are more credible and more general than the schema put forward by Paul [5], in which the intermediate stage in the synthesis of Δ^2-dihydropyran from tetrahydrofurfuryl alcohol involves the formation of methylenetetrahydrofuran (by dehydration of the alcohol), which is then isomerized to Δ^2-dihydropyran.

The schema we suggest for the mechanism involved in the expansion of a five-membered oxygen-containing, nitrogen-containing [6], or sulfur-containing heterocyclic compound to a six-membered one is supported and confirmed by one of the papers by N.M. Kizhner, who showed that the action of dehydrating agents upon complex carbinols isomerizes their rings and shifts their radicals. When dimethylcyclobutylcarbinol is reacted with oxalic or dilute sulfuric acid, we get 1,2- rather than 1,1-dimethylcyclopentene-1, the reaction involving the formation of the intermediate 1,1-dimethylcyclopentanol-2 [8]:



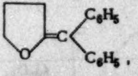
S.S. Nametkin has observed a similar phenomenon: when dimethylcyclopentylcarbinol was dehydrated by heating it with oxalic acid (by the N.M. Kizhner method), it yielded 1,2-dimethylcyclohexene-1:



In the instances cited the only possible reason for the shift of the methyl group is a retropinacol conversion of the resulting pinacol cyclic alcohol.

There is, therefore, no doubt that the intermediate substance present during the formation of Δ^2-dihydropyran from tetrahydrofurfuryl alcohol is not methylenetetrahydrofuran (a product of the dehydration of the alcohol), as R. Paul supposes, but α-hydroxytetrahydropyran, a product of the isomerization of the initial alcohol; the latter compound yields Δ^2-dihydropyran upon dehydration (Schema I).

Paul cites [10] the catalytic dehydration of diphenyltetrahydrofurylcarbinol, which does not entail isomerization and stops at the stage in which epoxy-1,4-5,5-diphenylpentene-4 (a compound with a heptacyclic double bond)



is formed,

as proof of the correctness of the schema given by him for the formation of Δ^2-dihydropyran from tetrahydrofurfuryl alcohol. S.S. Nametkin and M.A. Volodina have shown, however, that diphenylpentylcarbinol is dehydrated to a hydrocarbon containing a heptacyclic double bond, i.e., without any isomerization of the ring, which is in sharp contrast to dimethylcyclopentylcarbinol [11]. We assert that, inasmuch as epoxy-1,4-5,5-diphenylpentene-4, which has a styrene group (as has the dehydration product of diphenylcyclopentylcarbinol), is produced by dehydration of diphenyltetrahydrofurylcarbinol, it is quite obvious that the behavior of diphenyltetrahydrofurylcarbinol cannot be compared with that of tetrahydrofurfuryl alcohol in this reaction.

In the N.M. Kizhner and S.S. Nametkin reactions cited above we have a confirmation of the scheme we propose for the expansion of the ring involved in the splitting out of water from tetrahydrofurfuryl alcohol and α-hydroxymethylthiophane and in the splitting out of hydrogen sulfide from tetrahydrofurfurylthiol and α-mercaptomethylthiophane.

We attribute the absence of this thiol in the product of the reaction of tetrahydrofurfuryl alcohol with hydrogen sulfide to the transformation of the tetrahydrofurfurylthiol into Δ^2-dihydrothiopyran.

The yield of the Δ^2-dihydrothiopyran from the tetrahydrofurfurylthiol drops sharply as the reaction temperature is raised (22% at 300° and 2.3% at 380°); a similar phenomenon takes place when the temperature is raised in the catalytic dehydration of tetrahydrofurfuryl alcohol—in the synthesis of Δ^2-dihydropyran [12]—and in the catalytic synthesis of Δ^2-dihydrothiopyran from tetrahydrofurfuryl alcohol and hydrogen sulfide (27% at 300° and 11% at 350°). In every case decomposition increases sharply as the reaction temperature is raised, the catalyst being covered with a thick layer of carbon-like film.

After the present research had been completed, Naylor [13] published a paper on the use of a similar method in synthesizing Δ^2-dihydrothiopyran from tetrahydrofurfuryl alcohol, which combines in one reaction – as indicated above – the synthesis of Δ^2-dihydropyran [4] and the conversion of the latter into Δ^2-dihydrothiopyran, first described by one of the present authors [2]. The British author did not realize, however, that the transformations of functional derivatives of oxygen-containing heterocyclic compounds into rings containing other hetero atoms take place more easily than the transformations of their parental rings: furan, furanidine, Δ^2-dihydropyran and tetrahydropyran, so that fairly mild temperatures must be employed, avoiding any unnecessary rise in temperature. Naylor secured Δ^2-dihydrothiopyran from Δ^2-dihydropyran as well as from tetrahydrofurfuryl alcohol at excessively high temperatures: 425° and 375°, respectively, and in the presence of activated alumina into the bargain. That is why he secured a low yield of Δ^2-dihydrothiopyran containing tetrahydrothiopyran as an impurity in the first case, while in the second case the yield "was low" and the preparation "was somewhat impure".

Too high temperature and an excessively active catalyst merely promoted decomposition of the substance; the hydrogen evolved during decomposition could be added to the Δ^2-dihydrothiopyran produced by the cited author under such severe conditions, thus giving rise to the small amount of tetrahydrothiopyran found as an impurity in the principal reaction product.

In the present paper, as in the preceding one [2], the Δ^2-dihydrothiopyran was synthesized under much milder conditions. The fractionation data of the reaction products secured by reacting tetrahydrofurfuryl alcohol with hydrogen sulfide in the presence of alumina at 300 and 350° clearly show how this reaction is complicated when the temperature is raised: at 350° first runnings (which may also contain tetrahydrothiopyran) appear, distilling at 139-143.5°, though they are practically absent in the catalyzate secured at 300°.

The transformation of Δ^2-dihydropyran into Δ^2-dihydrothiopyran described earlier was also carried out under milder conditions (375°, unactivated alumina), which made it possible to avoid unnecessary decomposition and to secure Δ^2-dihydrothiopyran [2] containing no tetrahydrothiopyran.

EXPERIMENTAL

Synthesis of tetrahydrofurfurylthiol. The tetrahydrofurfurylthiol was prepared by reacting the sodium salt of tetrahydrofurfurylsulfuric acid with potassium hydrosulfide. 40 g of tetrahydrofurfuryl alcohol was stirred vigorously and chilled while 28 ml of concentrated H_2SO_4 was added. After this chilling of the reaction mass, ice was added to it, and then anhydrous soda (about 40 g) was added portionwise until the reaction was neutral. After the solution of the sodium salt of tetrahydrofurfurylsulfuric acid had stood for 10-15 hours, the crystals of Glauber salt were filtered out, and the filtrate was evaporated until a film appeared and then mixed with a solution of 17 g of potassium hydroxide in 34 ml of water, saturated with hydrogen sulfide. The reaction mixture was refluxed for 6-8 hours on an oil bath, and the reaction products distilled. This yielded a distillate passing over up to 115° and consisting of water and about 10 ml of a heavy colorless oil, which was extracted with ether. The ether extract was re-treated with a potassium hydroxide solution. The alkaline solution of potassium mercaptide was separated, extracted a few times with ether, and acidulated with hydrochloric acid after the ether had been driven off. Distillation of the residue left after the ether solution had been dried with anhydrous Na_2SO_4 and the ether had been driven off yielded 6.0 g of tetrahydrofurfurylthiol, with a b.p. of 167-169° (746 mm).

The residue left in the reaction flask was acidulated with hydrochloric acid. The upper layer was separated and extracted with ether. After the ether had been driven off, the residue was distilled, the distillate collected in the 95-320° range being treated with a solution of potassium hydroxide. The appropriate treatment of an alkaline solution of the potassium mercaptide yielded 1 g of tetrahydrofurfurylthiol, with a b.p. of 167-168° at 744 mm.

After the tetrahydrofurfurylthiol had been redistilled, it had the following constants:

B.p. 170-170.5° at 752 mm; n_D^{20} 1.4875; d_4^{20} 1.0383; MR$_D$ 32.76; calculated 32.42.
Found %: C 50.87, 50.84; H 8.50, 8.49; S 27.05, 27.03. $C_5H_{10}OS$. Calc.%: C 50.82; H 8.52; S 27.12.

The yield was 6.5 g (14% of the theoretical). Tetrahydrofurfurylthiol is not described in the literature.

Synthesis of Δ^2-dihydrothiopyran from tetrahydrofurfuryl alcohol. a) 110 g of tetrahydrofurfuryl alcohol was passed over alumina at 300° in a current of hydrogen sulfide at the rate of 7-8 drops per minute. The resulting catalyzate was saturated with potassium hydroxide. After the alkaline solution had been separated, the catalyzate was again treated with a solution of potassium hydroxide and then extracted with ether. The ether extract of the catalyzate was dried with calcium chloride, the ether driven off, and the residue distilled into a column with an efficiency of 18 theoretical trays, which yielded the following fractions: I) b.p. 90-139°, 4.5 g; II) b.p. 139-143.5°, 0.1 g; III) b.p. 143.5-144° at 742 mm, 29 g; IV) 144-170°, 2 g; and V) b.p. 170-220°, 3.5 g. The residue left in the flask (21 g) consisted of tar.

Fraction III was Δ^2-dihydrothiopyran:

B.p. 143.5-144° at 742 mm; n_D^{20} 1.5318; d_4^{20} 1.0221; MR$_D$ 30.35; calculated 30.59. Melting point of the $HgCl_2$ compound (in alcohol) 109-110°.

Found %: C 59.91; 60.00; H 8.01, 8.03; S 31.95, 31.92. C_5H_8S. Calc.%: C 59.95; H 8.05; S 32.01.

The yield was 29 g (27% of the theoretical).

Figures in the literature for Δ^2-dihydrothiopyran: Yu.K.Yuryev, T.B.Dubrovina, and E.P.Tregubov [2]: b.p. 143.6-144.2 at 743 mm; n_D^{20} 1.5328; d_4^{20} 1.0244.

The alkali solution with which the catalyzate had been treated was acidulated with hydrochloric acid and extracted with ether. The ether extract was dried with anhydrous Na_2SO_4, and the ether was driven off, leaving 0.1 g of a substance that did not exhibit a reaction for the sulfhydryl group. Hence, the catalyzate did not contain a thiol.

b) 200 g of tetrahydrofurfuryl alcohol was passed over alumina at 350° in a current of hydrogen sulfide at 7-8 drops/min. This yielded 138 g of catalyzate, which was processed as described above and then distilled into a column with an efficiency of 18 theoretical trays. Double fractionation yielded the following fractions: I) b.p. 76-110°, 5 g; II) b.p. 110-125°, 3 g; III) 125-139°, 0.6 g; IV) b.p. 139-143.5°, 3.5 g; V) b.p. 143.5-145°, 21 g; VI) b.p. 145-153°, 2 g; VII) b.p. 153-174°, 0.8 g. The residue in the flask, tar, totaled 32 g.

Fraction V was Δ^2-dihydrothiopyran (11% of the theoretical yield), b.p. 143.5-145° (755 mm); n_D^{20} 1.5328; d_4^{20} 1.0212; the $HgCl_2$ compound had a melting point (from alcohol) of 109-110°.

Conversion of tetrahydrofurfurylthiol into Δ^2-dihydrothiopyran. a) 27 g of tetrahydrofurfurylthiol was passed over alumina at 300° in a current of nitrogen at the rate of 7-8 drops/min. The 12.5 g of catalyzate was extracted with ether. After the ether extract had been dried with anhydrous Na_2SO_4 and the ether had been driven off, distillation of the reaction product from a flask fitted with a dephlegmator yielded the following fractions: I) b.p. 115-139°, 6.4 g; II) b.p. 139-148°, 5.4 g; III) b.p. 148-220°, 6.1 g. Redistillation of Fractions I and II into a column with an efficiency of 18 theoretical trays yielded 5.2 g of Δ^2-dihydrothiopyran (22% of the theoretical yield):

B.p. 143-144.5° at 742 mm; n_D^{20} 1.5318; d_4^{20} 1.0232. M.p. of the $HgCl_2$ compound (from alcohol): 109-110°.

Found %: C 59.98, 59.92; H 8.00, 7.97; S 31.89, 31.94. C_5H_8S. Calc.%: C 59.95; H 8.05; S 32.01.

b) 20 g of tetrahydrofurfurylthiol was passed over alumina at 380° in a current of nitrogen (at a rate of 7-8 drops/min.) After the gaseous reaction products had passed through a wash bottle filled with sodium plumbite, they were collected in a gasometer. The abundant black precipitate of lead sulfide indicated that hydrogen sulfide was present in the gases. 2300 ml of gas was collected (after the nitrogen introduced had been deducted). The 7.6 g of catalyzate was treated as in the preceding experiment. Redistillation of the reaction product from a flask fitted with a dephlegmator yielded 0.4 g of Δ^2-dihydrothiopyran (2.3% of the theoretical yield).

B.p. 143-144.5° at 745 mm; n_D^{20} 1.5312; d_4^{20} 1.0216. M.p. of the $HgCl_2$ compound (from alcohol) 109-110°.

Analysis of the gaseous reaction products yielded the following results: 42.4% unsaturated hydrocarbons; 20.2% saturated hydrocarbons; 37.2% carbon monoxide.

SUMMARY

1. When tetrahydrofurfuryl alcohol is reacted with hydrogen sulfide above alumina at 300°, the ring is first expanded, Δ^2- dihydropyran being produced; the action of hydrogen sulfide upon the latter converts it into Δ^2-dihydrothiopyran.

2. When tetrahydrofurfurylthiol is brought into contact with alumina at 300°, its ring is expanded, yielding Δ^2-dihydrothiopyran.

3. The functional derivatives of the furanidine series – tetrahydrofurfuryl alcohol and tetrahydrofurfurylthiol – are transformed at lower temperatures and, hence, more readily than the transformations of furanidine (tetrahydrofuran) and of its homologs.

4. The rings of the five-membered heterocyclic compounds that contain functional groups — tetrahydrofurfuryl alcohol, tetrahydrofurfurylthiol, α-hydroxymethylthiophane, and α-mercaptomethylthiophane — are expanded when they are brought into contact with alumina in accordance with a mechanism that holds good for them all: first, isomerization to a six-membered heterocyclic compound with the same hetero atom and with a hydroxyl or sulfhydryl group attached to the α-carbon atom, followed by splitting out of a molecule of water or hydrogen sulfide, respectively, yielding a six-membered Δ^2-unsaturated heterocyclic compound containing the same hetero atom.

When the hydrogen sulfide is split out from the tetrahydrofurfurylthiol, it reacts at once with the resultant Δ^2-dihydropyran in the presence of Al_2O_3, substituting sulfur for the oxygen. This is how Δ^2-dihydrothiopyran is formed from tetrahydrofurfurylthiol by placing the latter in contact with Al_2O_3.

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Received June 23, 1950

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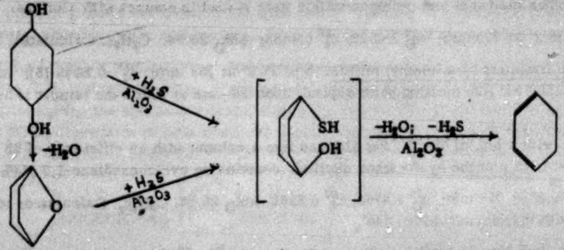
THE CATALYTIC DEHYDRATION OF 1,4-ENDOXOCYCLOHEXANE AND 1,4-DIHYDROXYCYCLOHEXANE IN AN ATMOSPHERE OF HYDROGEN SULFIDE

Yu K Yuryev, G.Ya Kondratyeva, and E.P.Smyslova

In our previous reports we have found that 2,2,5,5-tetramethylfuranidine is converted into 2,5-dimethylhexadiene-2,4 (diisocrotyl), a diene hydrocarbon with conjugated double bonds, instead of 2,2,5,5-tetramethylthiophane, by reacting it with hydrogen sulfide over alumina at 350° [1]. When 2,2,5,5-tetramethylfuranidine was dehydrated catalytically under the same conditions, but with hydrogen sulfide absent, we got a mixture that contained 2,5-dimethylhexadiene-1,5 (diisobutenyl), 2,5-dimethylhexene-2 (the cis and trans isomers), and possibly 2,5-dimethylhexane, in addition to 2,5-dimethylhexadiene-2,4 [2]. We were unable to separate the hydrocarbon mixture into its components, even by distilling the reaction product twice into a column with an efficiency of 25 theoretical trays, and the composition of the mixture was investigated by analyzing the Raman spectra of narrow fractions.

In the present research we made a study of the joint dehydration of 1,4-endoxocyclo- and 1,4-dihydroxycyclohexane with hydrogen sulfide over alumina with the objective of synthesizing 1,4-endothiocyclohexane. Even in this case, however, we secured a diene hydrocarbon, cyclohexadiene-1,3, rather than a sulfur-containing heterocyclic compound. Apparently, as in the case of 2,2,5,5-tetramethylfuranidine, which is formed as an intermediate from 1,4-endoxocyclohexane and 1,4-dihydroxycyclohexane (by the action of hydrogen sulfide), the disecondary mercapto hydroxy compound split out both water and hydrogen sulfide, yielding cyclohexadiene-1,3:



The impossibility of producing 1,4-endothiocyclohexane in the reactions described above is apparently due to the potential arising in a bicyclic molecule when the bridge oxygen is replaced by sulfur, which has a larger atomic radius.

EXPERIMENTAL

1,4-Endoxocyclohexane was produced by dehydrating 1,4-cyclohexanediol over alumina. 22 g of 1,4-cyclohexanediol and 15 g of Al_2O_3 were heated to 240-250° for 20 hours on an oil bath; the reaction product distilled slowly, drop by drop, into the receiver. The distillate was saturated with potash and extracted with ether. The ether was driven off, the ether extract dried with fused potash, and the residue distilled from a flask with a dephlegmator. 22 g of 1,4-dihydroxycyclohexane yielded 9 g of the crude oxide (48 % of the theoretical yield) with a b.p. of 115-119° at 735 mm. Redistillation of 45 g of the oxide over sodium yielded 42 g of pure 1,4-endoxocyclohexane:

B.p. 118.118.5 at 748 mm; n_D^{20} 1.4490; d_4^{20} 0.9731; MR_D 27.05. $C_6H_{10}O$. Calculated: MR_D 27.15.

Data in the literature for 1,4-endoxocyclohexane: b.p. 120.1°; n_D^{20} 1.4477; d_4^{20} 0.9707 [3].

The same yield of 1,4-endoxocyclohexane was secured when a mixture of 1,4-dihydroxycyclohexane and methanol was passed over alumina [3].

Catalytic dehydration of 1,4-endoxocyclohexane in an atmosphere of hydrogen sulfide. 10 g of 1,4-endoxocyclohexane was passed over alumina at 275° in a current of hydrogen sulfide at a rate of 18 ml per hour. The resultant catalyzate was extracted with ether; the ether extract was washed with a solution of sodium hydroxide and then dried with calcium chloride. After the ether was driven off, the residue was distilled twice from a flask fitted with a dephlegmator. The following fractions were collected in the second distillation: 1) b.p. 50-78°, 0.5 g; and 2) b.p. 78.5-79.5° at 749 mm, 1.8 g. Fraction 2 possessed the following constants:

B.p. 78.5-79.5° at 749 mm; n_D^{20} 1.4760; d_4^{20} 0.8453; MR_D 26.74. $C_6H_8F_2$. Calculated: MR_D 26.77.

These constants are quite close to those of cyclohexadiene-1,3, for which the literature gives a b.p. of 78.3-78.8° at 727 mm; d_4^{20} 0.8406; n_D^{20} 1.4744 [4]. To prove that the synthesized preparation actually was cyclohexadiene-1,3, it was reacted with maleic anhydride, 0.479 g of the hydrocarbon being heated with 0.421 g of maleic anhydride for an hour and a half on a water bath (while being agitated) in a flask fitted with a reflux condenser. After standing for a day, the excess hydrocarbon was driven off in vacuo (by heating on a water bath), and the precipitated crystals were washed a few times with boiling water to eliminate the unreacted maleic anhydride. Drying and double recrystallization from petroleum ether yielded crystals with a m.p. of 145-146°, which is exactly the melting point of Δ^4-3,6-endoethylenetetrahydrophthalic anhydride [5]. Its mixed melting point with Δ^4-3,6-endoethylenetetrahydrophthalic anhydride exhibited no depression.

This proved that the principal reaction product when 1,4-endoxocyclohexane is dehydrated in a current of hydrogen sulfide over Al_2O_3 was cyclohexadiene-1,3.

Catalytic dehydration of 1,4-dihydroxycyclohexane in an atmosphere of hydrogen sulfide. 60 g of 1,4-dihydroxycyclohexane, dissolved in 48 ml of methanol, was passed over Al_2O_3 at the rate of 21.5 ml per hour. The 73 g of condensate, which consisted of two layers, was collected in a well-chilled receiver and saturated with alkali; the upper layer (46.5 g) was separated, washed with water, dried, and distilled in a flask fitted with a dephlegmator. The first distillation yielded the following fractions: 1) b.p. 33-45°, 9 g; 2) b.p. 45-72°, 0.8 g; 3) b.p. 72-84°, 18.5 g; 4) b.p. 84-100°, 2 g; the high-boiling reaction products were distilled without a dephlegmator: 5) b.p. 100-160°, 6.2 g; 6) b.p. 160-250°, 1.3 g; the 4.2 g of residue crystallized upon standing. Fraction 1 (b.p. 33-45°), which had the acrid odor of sulfur compounds, was redistilled with a tall dephlegmator, almost all of it distilling at 37.8-38.2° at 760 mm. The substance yielded a crystalline compound with $HgCl_2$ (by pouring it into an alcoholic solution of mercuric chloride) with a m.p. of 162°. The resultant preparation (8 g yield, or 18% of the theoretical) was dimethyl sulfide, produced when methanol and hydrogen sulfide were placed in contact with alumina:

B.p. 37.8-38.2° at 760 mm; n_D^{20} 1.4578; d_4^{20} 0.8456; MR_D 20.04. C_2H_6S. Calculated: MR_D 19.40.

Data in the literature for dimethyl sulfide: b.p. 37.2° at 758 mm; d_4^{20} 0.8449 [6]; melting point of the $HgCl_2$ compound: 150-151° (the melting point depends upon the rate at which the sample is heated and may rise as high as 170° [7].

Fraction 3, with a b.p. of 72-84°, was distilled into a column with an efficiency of 25 theoretical trays. At 79.6-79.8° (756 mm), 18 g of the hydrocarbon distilled, constituting cyclohexadiene-1,3 (44% of theoretical yield):

B.p. 79.6-79.8° at 756 mm; n_D^{20} 1.4760; d_4^{20} 0.8386; MR_D 26.95. $C_6H_8F_2$. Calculated: MR_D 26.77. M.p. of the addition product with maleic anhydride: 146°.

Data in the literature for cyclohexadiene-1,3: b.p. 80.5°; d_4^{20} 0.8376 [8]; b.p. 78.3-78.8° at 727 mm; d_4^{20} 0.8406; n_D^{20} 1.4744 [9]; b.p. 78-79°;) d_4^{20} 0.8410; n_D^{20} 1.4739; m.p. of the addition product with maleic anhydride: 147° [5].

SUMMARY

1. When 1,4-endoxocyclohexane is passed over Al_2O_3 at 275° in an atmosphere of hydrogen sulfide, the oxide is dehydrated and cyclohexadiene-1,3 is formed.

2. Catalytic dehydration of 1,4-dihydroxycyclohexane over alumina in an atmosphere of hydrogen sulfide likewise results solely in cyclohexadiene-1,3.

3. The sulfur compound corresponding to 1,4-endocyclohexane, 1,4-endothiocyclohexane, is not produced by either 1,4-endoxocyclohexane or 1,4-dihydroxycyclohexane in the transformation of these heterocyclic compounds.

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Received July 13, 1950

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THE N-ARYL AMIDES OF HYDROXY CARBOXYLIC ACIDS AND THEIR CONVERSION INTO HETEROCYCLIC COMPOUNDS

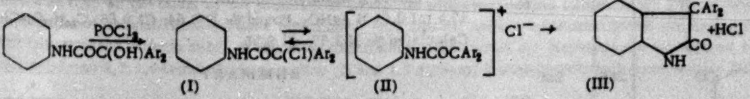
XIII USE OF VARIOUS DEHYDRATING AGENTS IN THE INTRAMOLECULAR CONDENSATION OF ARYL AMIDES OF α-HYDROXY CARBOXYLIC ACIDS

P.A.Petyunin

The following compounds: $AlCl_3$, $ZnCl_2$, $POCl_3$, HSO_3Cl, $(CH_3CO)_2O$, and CH_3COCl, have been used in addition to sulfuric, phosphoric, and hydrochloric acids, as condensing agents in the intramolecular condensation of aryl amides of α-hydroxy carboxylic acids.

In the presence of anhydrous aluminum chloride the reaction mass was strongly tarred, and we were unable to isolate the condensation product in the pure state. When chlorosulfonic acid is present, condensation is probably paralleled by a deeper change in the substance. An orange-red product was secured, its color changing as the pH of the medium changes. Anhydrous zinc chloride can be used for the intramolecular condensation of the aryl amides of α-hydroxy carboxylic acids (Experiment 1). It is not as suitable as concentrated sulfuric acid, however, as the reaction requires a high temperature and a longer time, while the reaction product is less pure and the yield is lower. The results of our experiments are listed in the table below. Aryl amides do not condense in the presence of acetic anhydride or acetyl chloride (these tests were run at the boiling points of the condensing agents).

Compounds of the $ArNHCOC(OH)Ar'_2$ type were used in the tests of phosphorous oxychloride, where Ar = C_6H_5 and β-$C_{10}H_7$; and Ar' = C_6H_5 and $C_6H_4OCH_3$-p. When the aryl amide's basicity is high enough (producing halochromic salts with HCl or H_3PO_4, the aryl amide of the diarylchloroacetic acid (I) produced when the initial aryl amide is reacted with $POCl_3$ dissociates to form a colored halochromic salt (II). Then the heterocyclic ring is closed (III) (Experiment 2) and HCl is liberated:



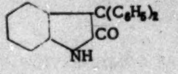
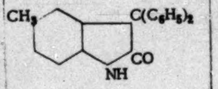
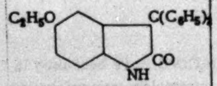
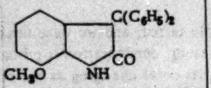
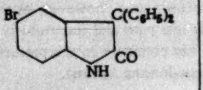
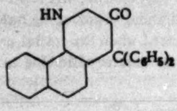
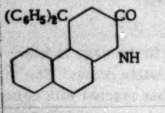
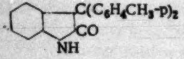
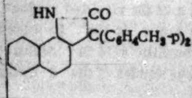
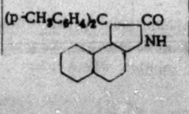
When the aryl amides do not form onium salts with these acids, the reaction stays in the stage in which aryl amides of diphenylchloroacetic acid (I) are produced (Experiments 3 and 4), and no condensation occurs. The aryl amides of diphenylchloroacetic acid are halochromic: they give off hydrogen chloride when reacted with concentrated sulfuric acid, producing red solutions that become decolorized upon standing. The ability of the aryl amides of diphenylchloroacetic acid to form halochromic salts is evidence of the feasibility of converting them into heterocyclic compounds.

EXPERIMENTAL

3,3-Diphenyl-5-methyloxindole (Experiment 1). 0.5 g of the p-toluide of benzilic acid was heated with 0.5 g of anhydrous zinc chloride to 180-190° for an hour. After the molten mass had cooled, it was pulverized and treated with hot 75% alcohol. The extraction residue was air-dried. This yielded 0.4 g of the air-dried product, or 85.1% of the theoretical yield. It crystallized from toluene as colorless lamellae with a m.p. of 198°. Its mixed melting point with 3,3-diphenyl-5-methyloxindole, synthesized from the p-toluide of benzilic acid in concentrated sulfuric acid exhibited no depression. The intramolecular condensation of the other aryl amides of the α-hydroxy carboxylic acids was effected similarly.

Found %: N 4.77. $C_{21}H_{17}ON$. Calculated %: N 4.68.

3,3-Bis-(4-methoxyphenyl)-4,5-benzoxindole (3,3-bis-(4-methoxyphenyl)-β-naphthoxindole) (Experiment 2). 0.8 g of the β-naphthalide of 4,4'-dimethoxydiphenylglycolic acid was dissolved in 12 ml of toluene. 0.5 g of freshly distilled phosphorus oxychloride was added to the solution, producing a crimson solution, whose color

No.	Formula	M.p.	M.p. of the product obtained in H_2SO_4
1		225°	225-226°
2		198	197.5-198.5
3		250	250
4		270	270
5		284	284
6		253	254
7		266	266
8		200	200-201
9		220	220
10		246.5	246.5

intensity gradually increased. The reaction mass was heated for 10-15 min on a water bath until the crimson coloration disappeared completely. After the mixture had cooled the precipitate was filtered out and recrystallized from acetic acid. Colorless little stars with a m.p. of 270° [1]. Their mixed melting point with a known sample exhibited no depression. The yield was 0.5 g, or 59% of the theoretical.

Anilide of diphenylchloroacetic acid (Experiment 3). 4 ml of phosphorus oxychloride was poured over 4 g of benzilanilide, and the mixture was carefully heated on a water bath until dissolution was complete. When the reaction mass had cooled, it was poured into 100 ml of cold water, the resulting oil crystallizing when the mixture was stirred. This yielded 3 g or 70% of the theoretical. Crystallization from benzene yielded colorless needles with a m.p. of 88°. Klinger gives 88° [2]. The anilide dissolves in concentrated sulfuric acid, giving off hydrogen chloride and turning red, the color disappearing upon standing.

Found %. N 4.3; Cl 11.12. $C_{20}H_{16}ONCl$.

Calculated %: N 4.35; Cl 11.04.

The β-naphthalide of diphenylchloroacetic acid (Experiment 4). 2.5 g of the β-naphthalide of benzilic acid and 2.5 ml of phosphorus oxychloride were used for this reaction. The naphthalide dissolves with difficulty in cold gasoline, but readily in hot; It is soluble in benzene and carbon tetrachloride. It colors concentrated sulfuric acid a transient red-brown. Decolorization is accompanied by the evolution of hydrogen chloride. Triple crystallization from gasoline yielded colorless needles with a m.p. of 109°. The yield was 0.7 g, or 26.9% of the theoretical. The initial β-naphthalide of benzilic acid is produced when an aqueous suspension of the substance is allowed to stand at room temperature, this reaction being accelerated by heat.

0.2650 g substance: 13.8 ml 0.05 N H_2SO_4. 0.0643 g substance: 17.5 ml 0.01 N $AgNO_3$. Found %: N 3.64; Cl 9.66. $C_{24}H_{18}ONCl$. Calculated %: N 3.77; Cl 9.55.

SUMMARY

1. $AlCl_3$, $ZnCl_2$, HSO_3Cl, $POCl_3$, $(CH_3CO)_2O$ and CH_3COCl have been tested as condensing agents for converting the aryl amides of α-hydroxy carboxylic acids into heterocyclic compounds. It was found that anhydrous zinc chloride could be employed for this purpose. In contrast to sulfuric acid, however, the reaction with this chloride requires a higher temperature, while the product's purity and yield are lower. The aryl amides that form halochromic salts with hydrochloric or phosphoric acids are condensed by phosphorus chloride.

2. The reaction of phosphorus oxychloride with the anilide and β-naphthalide of benzilic acid indicates that the aryl amides of diphenylchloroacetic acid can be produced.

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Received
February 1, 1950

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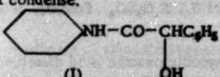
THE N-ARYL AMIDES OF HYDROXY CARBOXYLIC ACIDS AND THEIR CONVERSION INTO HETEROCYCLIC COMPOUNDS

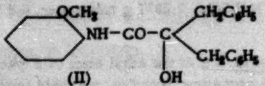
XIV. THE BOUNDARIES OF THE INTRAMOLECULAR CONDENSATION OF ARYL AMIDES OF HYDROXY CARBOXYLIC ACIDS

P.A.Petyunin

Aryl amides of rigidly specified structure enter into intramolecular condensations. The ability of aryl amides to enter into condensations is chiefly governed by the nature of the radicals attached to the carbinol carbon atom. The aryl amides of aliphatic α-hydroxy carboxylic acids do not condense, for example. Experiments were made with the anilides of glycolic and diisoamylglycolic acids. Concentrated sulfuric acid was added to an acetic acid solution of diisoamylglycolanilide, and the reaction mass was either allowed to stand for 12 hours at room temperature or heated for 1 hour on a water bath. In the first case the original aryl amide was recovered, while in the second hydrolysis occurred, yielding diisoamylglycolic acid and aniline. Experiments with glycolanilide yielded similar results. Moreover, fusing the latter with anhydrous zinc chloride likewise failed to yield satisfactory results.

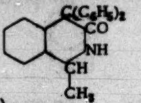
The aryl amides of hydroxy carboxylic acids in which one aromatic radical is attached to the carbonyl carbon atom (I) or in which there is no direct bond between the carbinol carbon atom and the benzene rings of the radicals (II), do not condense.


(I)


(II)

These aryl amides do not color concentrated sulfuric acid.

Numerous experiments have shown that the aryl amides that form halochromic salts with concentrated sulfuric acid do enter into condensation reactions. Hence, the ability of aryl amides to enter into intramolecular condensations may be governed by the presence of coloration with concentrated sulfuric acid. The α- and β-phenylethylamides of benzilic acid we have synthesized, for instance, produce ephemeral brown and dark-red colorations with concentrated sulfuric acid. When these experiments were carried out preparatively, we secured 1-methyl-4,4-diphenyl-3-oxo-1,2,3,4-tetrahydroisoquinoline (I) and 1,1-diphenyl-2-oxohomotetrahydroisoquinoline (IV):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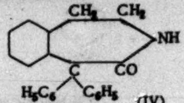

(IV)

Of the aryl amides of various hydroxy carboxylic acids we have tested, the compounds of the (VIII), (IX), and (X) types enter into intramoledular condensation. [See next page for (V) to (X)].

EXPERIMENTAL

Ethyl ester of α-phenylethyloxamic acid. When 16 g of α-phenylethylamine, prepared from acetophenone and ammonium formate [1], was mixed together with 24 g of ethyl oxalate, heat was evolved and a small crystalline precipitate was thrown down. Finally, the reaction mass was heated until its reaction was neutral. The contents of the flask were then poured into 50 ml of alcohol, and the precipitated di-(α-phenylethyl)-amide of oxalic acid was processed in the usual manner, yielding 2 g of the substance. The latter is insoluble in water, slightly soluble in alcohol and carbon tetrachloride, and freely soluble in acetic acid and toluene. It crystallizes from toluene as colorless needles with a m.p. of 195°. The literature gives the m.p. of the di-(α-phenylethyl)-amide of oxalic acid as 180-185° [2]. Driving off the alcohol left behind an oily liquid, which was distilled in vacuo at 213-215° (21 mm). It crystallized when allowed to stand overnight. Colorless needles (from benzene) with a m.p. of 51.5°. The yield was 10.5 g, of 38.2% of the theoretical. The ester is insoluble in water, though soluble in the usual organic solvents. The ethyl ester of α-phenylethyloxamic acid is not described in the literature.

0.2200 g substance: 20.4 ml 0.05 N H_2SO_4. Found%: N 6.48. $C_{12}H_{15}O_3N$. Calculated %: N 6.33.

Ethyl ester of β-phenylethyloxamic acid. 12 g of ethyl oxalate was added to a solution of 8 g of β-phenylethylamine in 20 ml of alcohol. The reaction was completed by heating the flask's contents on a water bath until they no longer manifested an alkaline reaction with litmus paper. This yielded 0.4 g of di-(β-phenylethyl)-amide of oxalic acid. Colorless needles (from alcohol) with a m.p. of 186°. The literature gives the m.p. as 186° [3].

Found%: N 9.29. $C_{18}H_{20}O_2N_2$. Calculated %: N 9.46.

The ethyl ester of β-phenylethyloxamic acid is insoluble in water, slightly soluble in gasoline, and readily soluble in other organic solvents. Colorless needles (from benzene) with a m.p. of 68°. The yield totalled 9 g, or 54.8% of the theoretical.

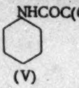
0.1302 g substance: 11.5 ml 0.05 N H_2SO_4. Found%: N 6.11. $C_{12}H_{15}O_3N$. Calculated%: N 6.33.

The o-aniside of dibenzylglycolic acid. We used 4.5 g of the ethyl ester of o-methoxyoxanilic acid, 10.1 g of benzyl chloride, and 1.9 g of magnesium for this reaction. The aniside is insoluble in water and freely soluble in ordinary organic solvents. It does not color concentrated sulfuric acid. Crystallization from alcohol yielded a finely crystalline powder with a m.p. of 150-151°. The yield totaled 4.1 g, or 55% of the theoretical.

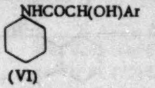
0.1916 g substance: 5.28 ml 0.1 N H_2SO_4. 0.2371 g substance: 6.8 ml 0.1 N H_2SO_4. Found%: N 3.86, 4.01. $C_{23}H_{23}O_3N$. Calculated %: N 3.88.

α-Phenylethylamide of benzilic acid. 4 g of the ethyl ester of β-phenylethyloxamic acid dissolved in 30 ml of absolute ether was reacted with phenylmagnesium bromide, prepared from 17 g of bromobenzene and 2.58 g of magnesium in 40 ml of ether. The yield of the recrystallized product totaled 3.7 g, or 58.3% of the theoretical. The substance is insoluble in water or gasoline, though freely soluble in alcohol, ether, and benzene. It colors concentrated sulfuric acid an ephemeral brown. It crystallizes from alcohol as colorless needles with a m.p. of 149.5-150.5°.

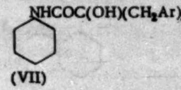
0.1448 g substance: 0.4217 g CO_2; 0.0832 g H_2O. 0.1035 g substance: 0.3012 g CO_2; 0.0601 g H_2O. 0.3956 g substance: 24.96 ml 0.05 N H_2SO_4. 0.1803 g substance: 10.9 ml 0.05 N H_2SO_4. Found %: C 79.47, 79.42; H 6.43, 6.5; N 4.39, 4.24. $C_{22}H_{21}O_2N$. Calculated %: C 79.72; H 6.39; N 4.23.



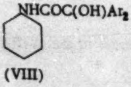
(V)



(VI)



(VII)



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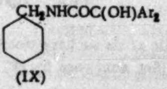

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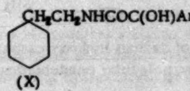

(X)

(R = H, alkyl; Ar = aryl).

β-Phenylethylamide of benzilic acid. Initial substances: 6 g of the ethyl ester of β-phenylethyloxamic acid, 33 g of iodobenzene, and 4 g of magnesium. The anilide is insoluble in water, slightly soluble in gasoline, and freely soluble in other organic solvents. It colors concentrated sulfuric acid dark red, the color changing to pale green. It crystallizes from alcohol as colorless lamellae with a m.p. of 139°. The yield totaled 5.3 g, or 65.7% of the theoretical.

0.1531 g substance: 0.4470 g CO_2; 0.0874 g H_2O. 0.1371 g substance: 0.4000 g CO_2; 0.0780 g H_2O. 0.1733 g substance: 10.4 ml 0.05 N H_2SO_4. 0.1926 g substance: 12.3 ml 0.05 N H_2SO_4. Found %: C 79.68, 79.62; H 6.39, 6.37; N 4.32, 4.47. $C_{22}H_{21}O_2N$. Calculated %: C 79.72; H 6.39; N 4.23.

1-Methyl-4,4-diphenyl-3-oxo-1,2,3,4-tetrahydroisoquinoline. 3 g of the α-phenylethylamide of benzilic acid was dissolved in 30 ml of glacial acetic acid, and 15 ml of concentrated sulfuric acid was added to the solution. After the red-brown coloration had disappeared, the reaction product was isolated in the usual manner. The substance is insoluble in water, slightly soluble in benzene, toluene, and gasoline, and readily soluble in alcohol and acetic acid. It crystallizes from dilute acetic acid as colorless rods with a m.p. of 272°.

0.1635 g substance: 0.5047 g CO_2; 0.0869 g H_2O. 0.1802 g substance: 0.5551 g CO_2; 0.0967 g H_2O. 0.1628 g substance: 10.12 ml 0.05 N H_2SO_4. 0.1876 g substance: 12 ml 0.05 N H_2SO_4. 0.0094 g substance: 0.1490 g camphor: Δt 8°. 0.0091 g substance; 0.1100 g camphor: Δt 10.8°. Found %: C 84.29, 84.06; H 5.95, 6; N 4.35, 4.48; M 315.5, 306.4. $C_{22}H_{19}ON$. Calculated %: C 84.4; H 6.12; N 4.47; M 313.

Lactam of o-(β-aminoethyl)-triphenylacetic acid (1,1-diphenyl-2-oxohomotetrahydroisoquinoline-symmetrical). Initial substances: a solution of 3.5 g of the β-phenylethylamide of benzilic acid in 20 ml of glacial acetic acid and 30 ml of concentrated sulfuric acid. Condensation was effected at 50-60°. The substance is insoluble in water, though it dissolves in most of the ordinary organic solvents. It crystallizes from alcohol as thin colorless needles with a m.p. of 187-189°. The yield totaled 2.7 g, or 84.6% of the theoretical.

0.1250 g substance: 0.3861 g CO_2; 0.0672 g H_2O. 0.1530 g substance: 0.4740 g CO_2; 0.0832 g H_2O. 0.2359 g substance: 14.5 ml 0.05 N H_2SO_4. 0.1761 g substance: 10.7 ml 0.05 N H_2SO_4. 0.0090 g substance: 0.0986 g camphor; Δt 11.8°. 0.0096 g substance; 0.1011 g camphor: Δt 12.4°. Found %: C 84.29, 84.55; H 5.97, 6.09; N 4.31, 425; M 309.6, 306.2. $C_{22}H_{19}ON$. Calculated %: C 84.4; H 6.12; N 4.47; M 313.

SUMMARY

The proximate boundaries of the intramolecular condensation of the N-aryl amides of hydroxy carboxylic acids have been determined, in so far as the nature of the radicals attached to the carbinol carbon atom are concerned.

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Received February 6, 1950

Laboratory of Organic Chemistry,
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SUMMARY

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LITERATURE CITED

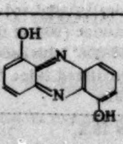
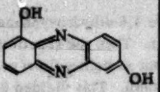
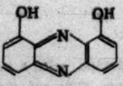
[illegible]

SYNTHESIS OF 1-HYDROXYPHENAZINE DERIVATIVES

III. 1,5-, 1,6-, AND 1,8-DIHYDROXYPHENAZINES

S.B.Serebryany

Not much research has been done on the dihydroxyphenazines. Three of the ten possible isomers have been described in the literature: the 1,2- [1], 2,3- [2], and 1,4-dihydroxyphenazines [3]. It has recently been shown [4,6] that the dihydroxyphenazine produced by hydrogenating iodinin catalytically is 1,5-dihydroxyphenazine [5]. The synthesis of 1,5-, 1,6-, and 1.8-dihydroxyphenazines is described in the present report. We secured these preparations by dealkylating the respective dialkoxyphenazines described by us earlier [6,7]. The properties of the new dihydroxyphenazines are given in the table.

No.	Name	Formula	M.p.	M.p. of the diacetyl derivative
I	1,5-Dihydroxyphenazine		280-281°	240-241°
II	1,6-Dihydroxyphenazine		305-306 (with decomposition)	148-149
III	1,8-Dihydroxyphenazine		296-297 (with decomposition)	257-258

The dihydroxyphenazines listed in the table are well-crystallized substances. They dissolve with very great difficulty in water and fairly difficultly in cold alcohol and benzene. When they are dissolved in dilute alkalies, they produce orange and red phenazinolates. Adding ferric chloride to an alcoholic solution of 1,5-dihydroxyphenazine colors it green. Solutions of the dihydroxyphenazines in dilute mineral acids are orange and red.

The phenazinols readily form well-crystallized diacetyl derivatives.

We are indebted to Prof.A.I. Kiprianov for his valuable counsel.

EXPERIMENTAL*

1,5-Dihydroxyphenazine. 1.8 g of 1,5-diethoxyphenazine, with a m.p. of 184-186° [6] was heated for 5 hours to 130-140° in a sealed tube together with 24 ml of 45% hydrobromic acid. The reaction mixture was treated with an excess of a 10% sodium hydroxide solution, thus producing a cherry-red phenazinolate. The solution was heated to boiling, filtered, and treated with an excess of 30% acetic acid. The dihydroxyphenazine settled out as a yellow-green amorphous precipitate. The precipitate was filtered out and dried. The contaminated product was refined by converting it into a diacetyl derivative. The crude dihydroxyphenazine was boiled with 8 ml of acetic anhydride. Upon cooling the diacetoxyphenazine crystallized as yellow needles with a greenish tinge. The yield was 1.5 g of the substance, with a m.p. of 228-230°. After the acetic anhydride had been driven off, the mother liquor yielded another 0.1 g of the diacetate with a m.p. of 226-230°. The 1,5-diacetoxyphenazine was refined by crystallizing it from alcohol, 1.6 g of the contaminated diacetate yielding 1.4 g of the pure substance with a m.p. of 232-234°. This product was reconverted into 1,5-dihydroxyphenazine by saponifying it with an aqueous solution of an alkali. 1.4 g of the 1,5-diacetoxyphenazine and 15 ml of alcohol were boiled with 75 ml of a 5% sodium hydroxide solution. The precipitate dissolved within 30 minutes, the solution turning cherry-red. The hot solution was filtered and treated with a slight excess of acetic acid. The 1,5-dihydroxyphenazine crystallized as minute yellow needles. They were filtered out, washed with water, and dried. The yield totaled 0.95 g, or 70%, based on the diethoxyphenazine used.

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* The melting points of the pure preparations are corrected.

Crystallization from benzene yielded 0.86 g of pure 1,5-dihydroxyphenazine. Golden-yellow needles with a m.p. of 280-281° (in a sealed capillary).

Found %: N 13.24, 13.40. $C_{12}H_8O_2N_2$. Calculated %: N 13.2.

The pure 1,5-dihydroxyphenazine was converted into its diacetyl derivative, 0.18 g of the dihydroxyphenazine yielding 0.23 g of the diacetate with a m.p. of 234-235°. The preparation was recrystallized from alcohol for analysis. Light-yellow needles with a m.p. of 240-241°.

Found %: N 9.55, 9.61. $C_{16}H_{12}O_4N_2$. Calculated %: N 9.46.

1,5-Dihydroxyphenazine can also be produced, with a high yield, by dealkylating a 1,5-dialkoxyphenazine with 65-70% sulfuric acid. 0.9 gram of 1,5-diethoxyphenazine, with a m.p. of 182-184°, was dissolved in 27 ml of 70% sulfuric acid. The solution was refluxed on a paraffin bath at 176-180° for 30 minutes. Upon cooling, the solution was poured into 75 ml of water, treated with an excess of 20% sodium hydroxide, heated to boiling, filtered, and treated with a slight excess of 30% acetic acid. This precipitated the dihydroxyphenazine as minute yellow needles. Upon cooling 0.6 g of the substance was collected. The crude dihydroxyphenazine was purified by converting it into its diacetyl derivative (yielding 0.73 g of the diacetate with a m.p. of 230-232°), the diacetate being reconverted into 1,5-dihydroxyphenazine. Crystallization from benzene yielded 0.43 g of pure 1,5-dihydroxyphenazine (61% of the theoretical yield, based on the diethoxyphenazihe used). Golden-yellow needles with a m.p. of 280-281°. Its mixed melting point with the preparation described above exhibited no depression.

1,6-Dihydroxyphenazine. 0.68 gram of 1,6-diethoxyphenazine, with a m.p. of 151-152° [7], was dissolved in 20 ml of 70% sulfuric acid. The reaction product was dealkylated and processed as the 1,5-dihydroxyphenazine. This yielded 0.48 g of nearly pure 1,6-dihydroxyphenazine (90% of the theoretical yield, based on the 1,6-diethoxyphenazine used). Brown-yellow needles, m.p. 305-306° with decomposition (in a sealed capillary). A small quantity of the 1,6-dihydroxyphenazine was recrystallized twice from a benzene-absolute alcohol mixture for analysis. This produced no change in the melting point.

Found %: N 12.82, 12.85. $C_{12}H_8O_2N_2$. Calculated %: N 13.2.

1,6-Diacetoxyphenazine was produced from the pure 1,6-dihydroxyphenazine. 0.1 g of the dihydroxyphenazine was refluxed with 2 ml of acetic anhydride for 2 hours. Then the reaction mixture was poured into 100 ml of water. Some time later 1,6-diacetoxyphenazine settled out as light-yellow needles. The precipitate was filtered out, washed with water, and crystallized from 50% alcohol. This yielded 0.1 g of pure 1,6-diacetoxyphenazine; light-yellow needles with a m.p. of 148-149°.

Found %: N 9.50. $C_{16}H_{12}O_4N_2$. Calculated %: N 9.46.

1,8-Dihydroxyphenazine. 0.6 gram of 1,8-diethoxyphenazine, with a m.p. of 174° [7], was heated with 8.5 ml of hydrobromic acid in a sealed tube to 130-140° for 5 hours. The reaction product received the same treatment as the 1,5-dihydroxyphenazine. The 1,8-dihydroxyphenazine was secured as 0.48 g of minute yellow needles (almost the quantitative yield, based on the 1,8-diethoxyphenazine employed). The 1,8-dihydroxyphenazine was purified by converting it into the diacetate. 0.48 gram of the dihydroxyphenazine was boiled with 5.5 ml of acetic anhydride for 30 minutes. The dihydroxyphenazine dissolved at first, the diacetate settling out of the boiling acetic anhydride as yellow leaflets some 10-15 minutes later. After the acetic anhydride had cooled, 0.55 g of the diacetoxyphenazine, with a m.p. of 257-268°, was recovered. The preparation was pure and did not require crystallization. The 1,8-dihydroxyphenazine was regenerated from it, 0.55 g of the 1,8-diacetoxyphenazine and 10 ml of alcohol being boiled with 40 ml of a 5% sodium hydroxide solution until the deposit dissolved completely. The subsequent processing of the phenazinolate was the same as that used for the phenazinolate of 1,5-dihydroxyphenazine. This yielded 0.44 g of the dihydroxyphenazine, which was recrystallized from benzene. We secured 0.4 g of pure 1,8-dihydroxyphenazine (84% of the theoretical yield, based on the 1,8-diethoxyphenazine used). Clusters of orange needles with a m.p. of 286-287° with decomposition (in a sealed capillary).

Found %: N 13.01, 13.02. $C_{12}H_8O_2N_2$. Calculated %: N 13.2.

The 1,8-diethoxyphenazine was dealkylated rapidly and smoothly with 70% sulfuric acid, the yield being high. 1.35 g of 1,8-diethoxyphenazine, with a m.p. of 194° was dissolved in 40 ml of 70% sulfuric acid. The solution was refluxed for 30 minutes over a paraffin bath at 180-182° and then poured into 150 ml of water, its subsequent processing being the same as that employed for the 1,5-dihydroxyphenazine. This yielded 1.02 g of 1,8-dihydroxyphenazine (97% of the theoretical yield, based on the diethoxyphenazine employed); its m.p. was 291-

292°. The preparation was purified by extraction with benzene in a Soxhlet apparatus, followed by crystallization from benzene. This yielded 0.83 g of the pure substance, which crystallized as clusters of orange needles; m.p. 296-297° (in a sealed capillary).

This preparation was used in preparing 1,8-diacetoxyphenazine, yellow leaflets with a m.p. of 257-258°. The preparations of 1,8-diacetoxyphenazine produced by dealkylating 1,8-diethoxyphenazine with hydrobromic and sulfuric acids had the same melting point, while their mixed melting point exhibited no depression.

The 1,8-diacetoxyphenazine was crystallized from alcohol for analysis. Yellow leaflets with a m.p. of 257-258°.

Found %: N 9.68, 9.50. $C_{16}H_{12}O_4N_2$. Calculated %: N 9.46.

SUMMARY

1,5-, 1,6-, and 1,8-dihydroxyphenazines have been synthesized by dealkylating the respective dialkoxyphenazines with hydrobromic acid or 70% sulfuric acid.

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Received July 15, 1950.

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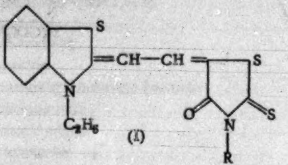
MEROCYANIN DYES THAT ARE DERIVATIVES OF RHODANINE

III. DIMETHINEMEROCYANINS — THE DERIVATIVES OF 3-AMINO- AND 3-DIACETYLAMINORHODANINE

Z. P. Sytnik, S. V. Natanson, M. V. Deichmeister, and L. D. Zhilina

We have previously shown [1] that substituting an alkyl group for the hydrogen atom attached to the nitrogen atom of the thiazolidine ring of the merocyanins — derivatives of rhodanine — such as (I) causes only a negligible shift of the dye's absorption maximum toward the longer wavelengths of the spectrum.



(I)

where R = H or C$_2$H$_5$.

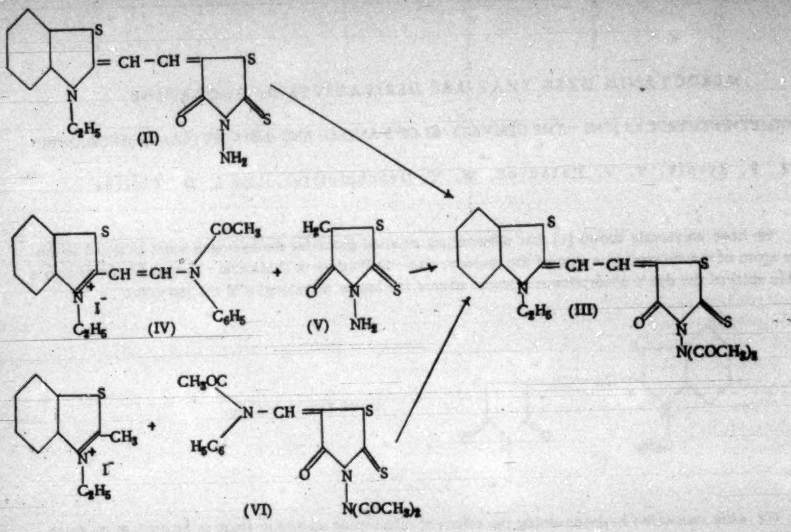
We were interested in determining the effect of substituting an amino group or an acylamino group for the hydrogen atom at that same position upon the properties of these dyes.

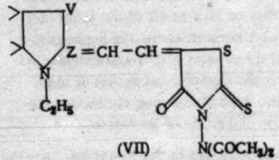
Of these dyes only a few amino substitution derivatives of the dimethinemerocyanins are mentioned in the patent literature [2]. The information given in these patents provides no idea at all of the properties of these compounds, however. We therefore synthesized analogous dyes with benzothiazole and benzoxazole (II) rings by condensing quaternary salts of acetanilinovinyl derivatives of these bases with 3-aminorhodanine in an alcoholic solution containing triethylamine [2]. Investigation of the photographic properties of these dyes has shown that the entrance of an amino group at the 3 position of the thiazolidine ring diminishes the sensitizing action, compared to that of the corresponding derivatives of the unsubstituted rhodanine.

No merocyanins with an acylated amino group at this position are described in the literature. Analogous dyes might have been expected to be formed when the respective amino substitution derivatives (II) are acylated. As a matter of fact, when we heated 3-amino-5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolidinethion-(2)-one-(4) (II) with acetic anhydride and anhydrous sodium acetate, we secured a dye that was the diacetylamino derivative (III) according to its analysis data. We secured a high yield of the same dye by condensing the ethiodide of 2-(β-acetanilinovinyl)-benzothiazole (IV) with 3-aminorhodanine (V) in acetic anhydride containing anhydrous sodium acetate by boiling them together for a short time (5-7 minutes). Increasing the heating time lowers the product yield. Lastly, a third method of synthesizing this dye involves the reaction of 3-diacetylamino-5-(acetanilinomethylene)-rhodanine (VI) with 2-methylbenzothiazole ethiodide in an alcoholic solution containing triethylamine: (see diagram top of next page)

We are the first to have synthesized 3-diacetylamino-5-(acetanilinomethylene)-rhodanine (VI) from 3-aminorhodanine (V) and diphenylformamidine by heating the latter with acetic anhydride; adding sodium acetate greatly increases the yield of this compound.

The synthesized merocyanin (III), in contrast to the amino substitution derivative (II), was highly soluble and possessed greater sensitizing action than the corresponding dyes derived from unsubstituted rhodanine. In this connection we thought it would be interesting to investigate as broadly as possible the optical and photographic properties of the dimethylmerocyanins, the derivatives of 3-diacetylaminorhodanine. With this in view, we synthesized analogous dyes containing the following residues: thiazoline, 5-methylthiodiazole-(1,3,4), benzothiazole, benzoxazole, benzoselenazole, 3,3-dimethylindolenine, β-naphthoxazole, 6,7-tetramethylenebenzothiazole, alpha and beta naphthothiazoles, and quinoline-(2 and 4) (VII).





(VII)

where V = O, S, Se, $-CH=CH-$, or $C(CH_3)_2$, and Z = carbon or the $CH=CH-\overset{|}{C}=$ group (when the latter group is present, there is no V).

The absorption maxima[1] of these dyes are given in Table 1, together with the maxima for the corresponding merocyanins derived from unsubstituted rhodanine and 3-aminorhodanine.

As we see from the figures in this table, introducing amino and diacetylamino groups at the 3 position of a thiazolidine residue has very little effect upon the color of these compounds. In most of the dyes we tested, moreover, we found a slight bathochromic shift (of some 2-6 mμ) of the same order of magnitude as found in the 3-ethylrhodanine [1], while the dyes that contain quinoline-(2 or 4) residues exhibit a slight displacement of the absorption maximum toward the shorter wavelengths (by some 4-6 mμ).

The slight influence of amino and diacetylamino groups upon the color of the merocyanins indicates that these groups interact negligibly with a polymethine chromophore.

The entrance of a diacetylamino group at the nitrogen atom of a thiazolidine residue increases efficiency over that of the dyes derived from unsubstituted rhodanine. The thiazoline, benzoxazole, 6,7-tetramethylenebenzothiazole, and α-naphthothiazole derivatives display exceptionally high sensitizing action. Somewhat lower, but still rather high, is the efficiency of dyes containing benzothiazole, β-naphthothiazole, and 5-methylthiodiazole-(1,3,4) residues. The derivatives of quinoline-(2 and 4) and of 3,3-dimethylindolenine are very weak sensitizers, however. As has been said above, introducing an amino group at this position has a negative effect upon the efficiency of this series of merocyanins.

All the dimethinemerocyanins — derivatives of 3-diacetylaminorhodanine — tested by us are very highly soluble in alcohol.

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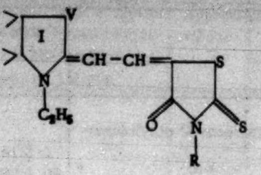
[1] The absorption curves of alcoholic solutions of these dyes were measured with a Koenig-Martens spectrophotometer.

TABLE 1



Variable residue (I)	Absorption maximum (mμ)		
	R		
	H	$N(COCH_3)_2$	NH_2
Thiazoline	480	479	–
5-Methylthiodiazole-(1,3,4).	511	512	–
Benzoxazole	488	492	492
β-Naphthoxazole.	502	507	–
Benzothiazole	520	526	526
6,7-Tetramethylenebenzothiazole	528	532	–
α-Naphthothiazole.	536	542	–
β-Naphthothiazole.	540	544	–
Benzoselenazole.	522	528	–
3,3-Dimethylindolenine	500	505	–
Quinoline-(2)	564	558	–
Quinoline-(4)	612	608	–

EXPERIMENTAL

Synthesis of intermediates. 3-Aminorhodanine [3]. A suspension of 22.6 g of trithiocarbodiglycolic acid in 300 ml of water was treated with small portions of sodium carbonate until its reaction was slightly alkaline (about 15-16 g of Na_2CO_3), after which 14 g of hydrazine sulfate was added to the solution, and the latter was heated for 3 hours in a boiling water bath. The next day the precipitate was filtered out and washed with water and alcohol. The yield totaled 5.9-6.7 g (40-45% of the theoretical); m.p. 90-91°. The m.p. of the product was 92-92.5° after recrystallization from alcohol. Yellow needles, rather freely soluble in alcohol.

3-Diacetylamino-5-(acetylanilinomethylene)-rhodanine. A mixture of 1.8 g of 3-aminorhodanine, 2.82 g of diphenylformamidine, 1.02 g of anhydrous sodium acetate, and 20 ml of acetic anhydride was boiled for 20 minutes. Upon cooling a crystalline precipitate settled out, which was filtered out and washed with water and then with alcohol. The yield totaled 1.75 g (43% of the theoretical); m.p. 200-203°. The yield totaled 1.32 g (32% of the theoretical) after recrystallization from ethyl alcohol. Minute, light-yellow needles with a m.p. of 205-206°.

Found %: N 11.08. $C_{16}H_{15}O_4N_3S_2$. Calculated %: N 11.13.

Synthesis of Dyes that are Derivatives of 3-Aminorhodanine

3-Amino-5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolidinethion-(2)-one-(4) [2]. A solution of 0.45 g of 3-aminorhodanine, 1.47 g of 2-(β-acetanilinovinyl)-benzothiazole ethiodide, and 0.42 g of triethylamine in 20 ml of absolute alcohol was boiled for 30 minutes. The next day the dye was filtered out and washed with alcohol and ether. The yield totaled 0.99 g (98.5% of the theoretical); m.p. 265° (with decomp.). Very slightly soluble in alcohol, so that it was refined by crystallization from pyridine. The yield was 0.7 g (69.5% of the theoretical). Brown needles with a green sheen; m.p. 276-277° (with decomp.).

Found %: N 12.32. $C_{14}H_{13}ON_3S_3$. Calculated %: N 12.22.

3-Amino-5-(3'-ethylbenzoxazolinylidene-2'-ethylidene)-thiazolidinethion-(2)-one-(4)[2]. This was synthesized, like the preceding dye, from 0.15 g of 3-aminorhodanine and 0.43 g of 2-(β-acetanilinovinyl)-benzoxazole ethiodide. The yield totaled 0.23 g (72.1% of the theoretical); m.p. 240-241° (with decomp.). Recrystalli-

TABLE 2

No.	Name of dye	Grams of I or II	Grams of specified quaternary salt	Condensation conditions	
				$(CH_3CO)_2O$ (ml)	CH_3COONa (g)
1	3-Diacetylamino-5-(3'-ethylbenzoxazolinylidene-2'-ethylidene)-thiazolidinethion-(2)-one-(4)	I; 0.15 II; 0.38	III; 0.43 XI; 0.34	2 –	0.09 –
2	3-Diacetylamino-5-(3'-ethylbenzoselenazolinylidene-2'-ethylidene)-thiazolidinethion-(2)-one-(4)	I; 0.15	IV; 0.5	2	0.09
3	3-Diacetylamino-5-(1'-ethyldihydroquinolylidene-2'-ethylidene)-thiazolidinethion-(2)-one-(4)	I; 0.15	V; 0.49	2	0.09
4	3-Diacetylamino-5-(1'-ethyldihydroquinolylidene-4'-ethylidene)-thiazolidinethion-(2)-one-(4)	I; 0.15	VI; 0.49	2	0.09
5	3-Diacetylamino-5-(1'-ethyl-3',3"-dimethylindolenylidene-2'-ethylidene)-thiazolidinethion-(2)-one-(4)	I; 0.15	VII; 0.45	2	0.09
6	3-Diacetylamino-5-(3'-ethyl-6',7'-tetramethylenebenzothiazolinylidene-2'-ethylidene)-thiazolidinethion-(2)-one-(4)	II; 0.38	XV; 0.39	–	–
7	3-Diacetylamino-5-(3'-ethyl-6',7'-benzobenzothiazolinylidene-2'-ethylidene)-thiazolidinethion-(2)-one-(4)	II; 0.38	XII; 0.4	–	–
8	3-Diacetylamino-5-(3'-ethyl-4',5'-benzobenzothiazolinylidene-2'-ethylidene)-thiazolidinethion-(2)-one-(4)	II; 0.38 I; 0.15	XIII; 0.4 X; 0.5	– 2	– 0.09
9	3-Diacetylamino-5-(3'-ethyl-4',5'-benzobenzoxazolinylidene-2'-ethylidene)-thiazolidinethion-(2)-one-(4)	I; 0.15	IX; 0.53	2	0.09
10	3-Diacetylamino-5-[3'-ethyl-5'-methylthiodiazolinylidene-(1', 3',4')-2'-ethylidene]-thiazolidinethion-(2)-one-(4)	I; 0.15	VIII; 0.4	2	0.09
11	3-Diacetylamino-5-(3'-ethylthiazolinylidene-2'-ethylidene)-thiazolidinethion-(2)-one-(4)	II; 0.38	XIV; 0.3	3 ml of pyridine	

zation from methanol (1:3000) yielded 0.2 g (62.6% of the theoretical). Light red, thin needles with a m.p. of 242° (with decomposition).

Found %: N 12.99, 12.86. $C_{14}H_{13}O_2N_3S_2$. Calculated %: N 13.12.

Synthesis of Dyes that are Derivatives of 3-Diacetylaminorhodanine

We give below a complete description of the synthesis of a merocyanin containing a benzothiazole residue, which was produced by three methods. All the other dyes of this series were synthesized similarly, by the second or third method. We therefore give their synthesis conditions, yields, melting points and analysis results in Table 3 for the sake of brevity.[1] In this table, the following notation is used for the initial products: 3-aminorhodanine – I; 3-diacetylamino-5-(acetanilinomethylene)-rhodanine – II; the ethiodides of 2-(β-acetanilinovinyl)-benzoxazole – III; of 2-(β-acetanilinovinyl)-benzoselenazole – IV; of 2-(β-acetanilinovinyl)-quinoline – V; of 4-(β-acetanilinovinyl)-quinoline – VI; of 3,3-dimethyl-2-(β-acetanilinovinyl)-indolenine – VII; and of 5-methyl-2-(β-acetanilinovinyl)-thiodiazole-(1,3,4) – VIII; the ethyl p-tolusulfonates of 2-(β-acetanilinovinyl)-β-naphthoxazole – IX; of 2-(β-acetanilinovinyl)-β-naphthothiazole – X, of 2-methylbenzooxazole – XI, of 2-methyl-α-naphthothiazole – XII, of 2-methyl-β-naphthothiazole – XIII, and of 2-methylthiazolidine – XIV; and the ethylbenzenesulfonate of 2-methyl-6,7-tetramethylenebenzothiazole – XV.

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[1] No Table 3 appears in the original Russian text. The publisher.

Condensation conditions			Yield, percent of theoretical	Ml of alcohol used in crystallizing 1 g of dye	Appearance of dye	M.p. with decomposition	Per cent N found	Calculated	
C_2H_5OH (ml)	$(C_2H_5)_3N$ (ml)	Boiling time, minutes						Empirical formula	Per cent N
– 7	– 0.14	5 30	66 46	300	Dark-pink needles	212-213	10.46; 10.61	$C_{18}H_{17}O_4N_3S_2$	10.46
–	–	5	66	600	Dark-red prisms	232-233	8.91; 8.97	$C_{18}H_{17}O_3N_3S_2Se$	9.00
–	–	5	30	250	Lustrous green lamellae	202	10.18	$C_{20}H_{19}O_3N_3S_2$	10.15
–	–	5	35	250	Green prisms	224	10.10; 9.92	$C_{20}H_{19}O_3N_3S_2$	10.15
–	–	5	40	60	Bright-red prisms	200	9.90	$C_{21}H_{23}O_3N_3S_2$	9.78
10	0.14	30	60	1000	Dark-red prisms	238-239	8.84; 9.03	$C_{22}H_{23}O_3N_3S_3$	8.85
10	0.14	30	50	1300	Dark-red prisms	237-238	8.76	$C_{22}H_{19}O_3N_3S_3$	8.94
10 –	0.14 –	30 5	46 42	1500	Minute brown needles	242-243	8.8	$C_{22}H_{19}O_3N_3S_3$	8.94
–	–	5	61	750	Light-red needles	255-256	9.39; 9.41	$C_{22}H_{19}O_4N_3S_2$	9.26
–	–	5	27	200	Lustrous red rhombic crystals	225-226	14.55 14.43	$C_{14}H_{16}O_3N_4S_3$	14.54
3 ml of pyridine		30	20	150	Lustrous orange lamellae	252-253	–	–	–

3-Diacetylamino-5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolidinethion-(2)-one-(4). This dye was synthesized in the three following ways.

a) A mixture of 0.167 g of 3-amino-5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolidinethion-(2)-one (4), 0.045 g of anhydrous sodium acetate, and 4 ml of acetic anhydride was boiled for 5 minutes. The yield of the dye was 0.15 g (71% of the theoretical) after recrystallization from alcohol. Violet needles with a green sheen; mp.224-225° (with decomp.).

(b) A mixture of 0.45 g of 2-(β-acetanilinovinyl)-benzothiazole ethiodide, 0.15 g of 3-aminorhodanine, 0.09 g of anhydrous sodium acetate, and 2 ml of acetic anhydride was boiled for 5 minutes. The dye was washed with water, alcohol, and ether, yielding 0.33 g (80% of the theoretical); m.p. 218-220° (with decomp.). Recrystallization from 150 ml of alcohol yielded 0.23 g (55% of the theoretical); m.p. 224-225° (with decomp.).

c) A solution of 0.38 g of 3-diacetylamino-5-(acetanilinomethylene)-rhodanine, 0.305 g of 2-methylbenzothiazole ethiodide, and 0.14 ml of triethylamine in 7 ml of absolute alcohol was boiled for 30 minutes. The dye was recrystallized from alcohol yielding 0.25 g (60% of the theoretical); m.p. 224-225° (with decomp.). The yield of the dye did not exceed 30% of the theoretical when the reaction was carried out in pyridine.

Found %: N 9.99, 10.12. $C_{18}H_{17}O_3N_3S_3$. Calculated %: N 10.01.

SUMMARY

1. A new group of dimethinemerocynanins — derivatives of 3-diacetylaminorhodanine, containing thiazoline, 5-methylthiodiazole-(1, 3, 4), benzoxazole, benzothiazole, benzoselenazole, 3,3-dimethylindolenine, 6,7-tetramethylenebenzothiazole, β-naphthoxazole, alpha and beta naphththiazole, and quinoline-(2 and 4) residues, has been synthesized.

2. These dyes, in contrast to the corresponding derivatives of unsubstituted rhodanine and 3-aminorhodanine, are highly soluble.

3. The optical and photographic properties of these dyes have been investigated.

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Received July 4, 1950.

All-Union Institute of Cinema and
Photographic Research

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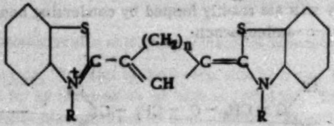
1) See Consultants Bureau English translation, p. 209.

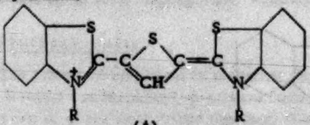
α, γ-EPOXYTHIACARBOCYANINS. I

I. K. Ushenko

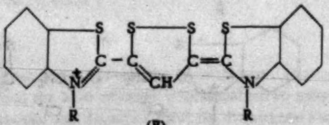
We have described [1] a series of thiacarbocyanins, the trimethine chromophore of which was part of the unsaturated ring:



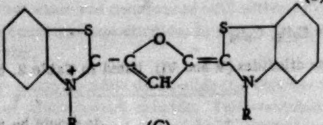
In the present research we set as our objective the introducing of sulfur and oxygen at the alpha and gamma positions:



(A)

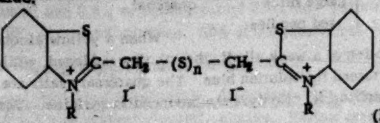


(B)



(C)

This was done by condensing thiodiglycolyl and dithiodiglycolyl chlorides with N-ethyl- and N-phenyl-o-aminothiophenol. The dichlorides were converted into the diiodides (I, II, III and IV) by the action of potassium iodide:



(I, II, III, IV)

The data on the diiodides (I, II, III, and IV) are set forth in Table 1.

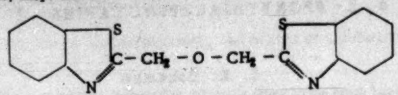
TABLE 1

No.	R	n	Melting point (with decomposition)
I	C_2H_5	1	146°
II	C_6H_5	1	198
III	C_2H_5	2	123
IV	C_6H_5	2	178

We assumed that heating these diquaternary salts with orthoformic ester in pyridine or acetic anhydride would yield dyes containing sulfur at the alpha and gamma positions (A) and (B). The condensation of the diquaternary salts with orthoformic ester in pyridine or acetic anhydride, however, yielded dyes that contained no sulfur at the alpha and gamma positions. Investigation of the properties (analysis, absorption curves in alcoholic solution, melting points) of mixed samples of the synthesized dyes indicated that when the salts (I) and (III) were heated with orthoformic ester, 3,3'-diethylthiacarbocyanin iodide was produced, while the salts (II) and (IV) yielded 3,3'-diphenylthiacarbocyanin iodide, which has been described earlier.

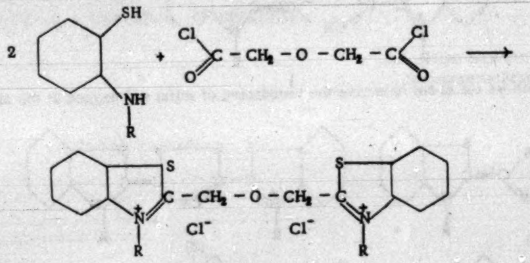
We have not tried to ascertain the mechanism of this condensation, involving the loss of sulfur atoms.

We found that it is fairly easy to synthesize cyanin dyes containing oxygen at the alpha and gamma positions (C). When o-aminothiophenol was heated with diglycolic acid, we got bis-[benzothiazolyl-(2)] oxide: large white scales, m.p. 105°:



We succeeded in transforming this base into a diquaternary salt by heating it with the ethyl ester of p-toluenesulfonic acid. The yield of the quaternary salt was extremely low.

The corresponding diquaternary salts are readily formed by condensing benzene solutions of diglycolyl chloride with N-ethyl-and N-phenyl-o-aminophenols:



R = C_2H_5, C_6H_5

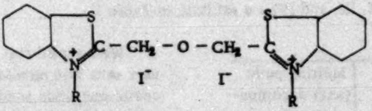
These salts were converted into the diiodides (V and VI), listed in Table 2, by the action of potassium iodide.

TABLE 2

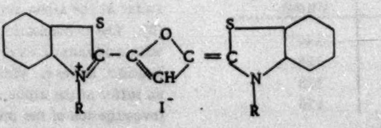
No.	R	Melting point	Appearance
V	C_2H_5	208°	Yellow needles
VI	C_6H_5	214	Large brick-red needles

It should be noted that the diquaternary salts remained brightly colored, in spite of their being refined by crystallization from alcohol or water and boiling with activated charcoal.

When a yellow alcoholic or pyridine solution of the salt (V) was exposed to the action of a weak alkali, the solution reddened, while the action of alkali upon the orange solution of the salt (VI) turned the solution blue. The quaternary salts are condensed fairly readily with orthoformic ester in acetic anhydride. No dyes are produced in pyridine. The two dyes (VII) and (VIII) listed in Table 3 were synthesized.



(V, VI)



(VII, VIII)

The absorption maxima of the dyes (VII) and (VIII) differ but little from the maxima of the corresponding carbocyanins, in which the oxygen atom in the four-membered ring has been replaced by a methylene group

TABLE 3

No.	R	Absorption maximum, mμ	$E_{max} \cdot 10^{-4}$
VII	C_2H_5	555*	13.2
VIII	C_6H_5	575	11.5

($R = C_2H_5$ – 560 mμ, $R = C_6H_5$ – 568 mμ). The synthesized dyes hardly fluoresce at all and readily decolorize alkalies and acids. Alcoholic solutions of the dyes are completely decolorized within 1-2 hours in bright sunlight. Their analogs, which contain a methylene group at the 8, 10 position, resist the action of light and alkalies rather well.

I. P. Dmitrenko, A. V. Stetsenko, and E. N. Rubtsova participated in the experimental portion of the present research.

EXPERIMENTAL

The acid chlorides of thiodiglycolic acid [2] and diglycolic acid [3] were prepared from the acids and phosphorus pentachloride.

The acid chloride of dithiodiglycolic acid [4] was prepared from dithiodiglycolic acid and thionyl chloride.

Bis-[benzothiazolyl-(2)]oxide. 5 grams of diglycolic acid (1 mole) was heated with 9.3 g of o-aminothiophenol (2 mole) in a sealed tube for 20 hours on an oil bath at 140-145°. The reaction product was processed with alkali and then with water. Double recrystallization from alcohol yielded large white scales, m.p. 105°, the yield being 6.2 g, or 55% of the theoretical.

Found %: N 9.12. $C_{16}H_{12}ON_2S_2$. Calculated %: N 8.97.

Diquaternary Salts

The procedure employed in preparing the diquaternary salts was the standard one. Equimolecular quantities of N-ethyl- or N-phenyl-o-aminothiophenol and the acid chloride were dissolved in anhydrous benzene, and the two solutions were mixed together. The benzene was decanted from the diquaternary salt produced, the residue being dissolved in hot water and decolorized with activated charcoal, after which the hot aqueous solutions of the chlorides were converted into diiodides by the action of potassium iodide. The salts were crystallized from alcohol or water.

Bis-[benzothiazolyl-(2)-methyl] sulfide diethiodide (I). This was synthesized from 5.7 g of N-ethyl-o-aminothiophenol and 3.5 g of thiodiglycolyl chloride. Yellow crystals from alcohol, which turned dark upon standing. M.p. 146° with decomposition. 27% of the theoretical yield.

Found %: I 38.42. $C_{20}H_{22}N_2S_3I_2$. Calculated %: I 39.68.

Bis-[benzothiazolyl-(2)-methyl] sulfide diiodophenylate (II). This was synthesized from 7.5 g of N-phenyl-o-aminothiophenol and 3.5 g of thiodiglycolyl chloride. Yellow crystals from alcohol, which darken upon standing. M.p. 198° with decomposition. 30% of the theoretical yield.

Found %: I 33.05. $C_{28}H_{22}N_2S_3I_2$. Calculated %: I 34.50.

Bis-[benzothiazolyl-(2)-methyl] disulfide diethiodide (III). This was synthesized from 2.2 g of N-ethyl-o-aminothiophenol and 1.6 g of dithiodiglycolyl chloride. Yellow crystals from alcohol. M.p. 122° with decomposition. 32% of the theoretical yield.

Found %: S 18.81. $C_{20}H_{22}S_4N_2I_2$. Calculated %: S 19.04.

Bis-[benzothiazolyl-(2)-methyl] disulfide diiodophenylate(IV). This was synthesized from 2.9 g of N-phenyl-o-aminothiophenol and 1.6 g of dithiodiglycolyl chloride. Minute yellow crystals. M.p. 178° with decomposition. 23% of the theoretical yield.

Found %: S 16.53. $C_{28}H_{22}N_2S_4I_2$. Calculated %: S 16.67.

Bis-[benzothiazolyl-(2)-methyl] oxide diethiodide (V). This was synthesized from 2 g of N-ethyl-o-aminothiophenol and 1.1 g of diglycolyl chloride. Yellow crystals from alcohol. M.p. 208° with decomposition. 43% of the theoretical yield.

Found %: I 40.23. $C_{20}H_{22}ON_2S_2I_2$. Calculated %: I 40.73.

Bis-[benzothiazolyl-(2)-methyl] oxide diiodophenylate (VI). This was synthesized from 2 g of N-phenyl-o-aminothiophenol and 0.9 g of diglycolyl chloride. Elongated red needles. M.p. 214° with decomposition. 61% of the theoretical yield. The preparation strongly irritates the mucous membrane of the nose.

Found %: I 35.22. $C_{28}H_{22}ON_2S_2I_2$. Calculated %: I 35.27.

Dyes

3,3'-Diethyl-8,10-epoxythiacarbocyanin iodide (VII). 0.4 g of bis-[benzothiazolyl-(2)-methyl] oxide diethiodide was boiled for 1 hour with 0.4 g of orthoformic ester and 2.5 ml of acetic anhydride. The dye was precipitated with ether. Recrystallization from alcohol yielded minute dark crystals. M.p. 198° with decomposition. The yield was 0.10 g, or 31% of the theoretical.

Found %: I 24.87. $C_{21}H_{19}ON_2S_2I$. Calculated %: I 25.09.

3,3'-Diphenyl-8,10-epoxythiacarbocyanin iodide (VIII). 1 g of bis-[benzothiazolyl-(2)-methyl] oxide diiodophenylate was boiled for 45 minutes with 1 g of orthoformic ester and 4 ml of acetic anhydride. The dye was precipitated with water. Recrystallization from alcohol yielded crystals with a bronze sheen. M.p. 178° with decomposition. The yield was 0.25 g, or 30% of the theoretical.

Found %: I 20.98. $C_{29}H_{19}ON_2S_2I$. Calculated %: I 21.09.

SUMMARY

1. Two diquaternary salts have been synthesized by condensing diglycolyl chloride with N-ethyl-and N-phenyl-o-aminothiophenol. Reacting them with orthoformic acid yielded two new dyes – α, β-epoxythiacarbocyanins.

2. Condensation of o-aminothiophenol with diglycolic acid yielded a new base – bis-[benzothiazolyl-(2)-methyl] oxide.

3. Four diquaternary salts were synthesized from N-ethyl- and N-phenyl-o-aminothiophenol and the thiodiglycolyl and dithiodiglycolyl chlorides; reacting these salts with orthoformic ester in acetic anhydride or pyridine detached sulfur atoms and gave rise to thiacarbocyanins that were unsubstituted in the trimethine chain.

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Received July 18, 1950

Institute of Organic Chemistry,
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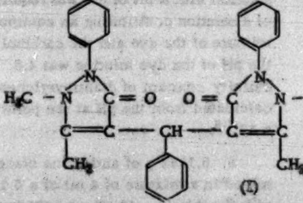
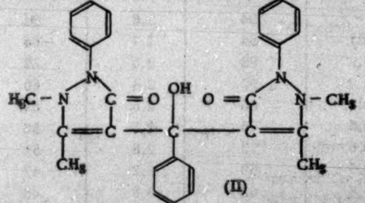
DYES WITH ANTIPYRINE RINGS. II

O. F. Ginzburg and B. A. Porai-Koshits

A few years ago we synthesized a new group of dyes, whose properties resembled those of basic triphenylmethane dyes, by oxidizing the condensation products of aromatic aldehydes with two molecules of antipyrine [1]. The simplest representative of this group of dyes, formed by the oxidation of diantipyrylphenylmethane, was obtained as a nitrate and was called antipyrine orange.

When an aqueous solution of antipyrine orange is reacted with an alkali solution, we get diantipyrylphenylcarbinol (II), which reconstitutes the dye when treated with acid.

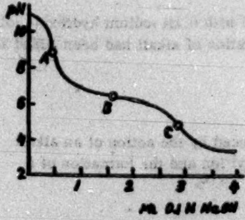

(I)


(II)

Diantipyrylphenylcarbinol is much more soluble in water than, say 4,4'-tetramethyldiaminotriphenylcarbinol, so that we can prepare a 0.001 molar aqueous solution of diantipyrylphenylcarbinol. We found that aqueous solutions of diantipyrylphenylcarbinol are readily colored, even if the solution contains a slight excess of free alkali.

The antipyrylphenylcarbinol solution, which contained a small percentage of sodium hydroxide, was titrated potentiometrically. In titrating this solution potentiometrically we found that after all the sodium hydroxide had been neutralized by adding hydrochloric acid, the solution pH, observed immediately after a new portion of hydrochloric acid had been added, gradually rose for a few minutes until it reached a certain value, after which it remained unchanged. Thus, the reaction of diantipyrylphenylcarbinol with hydrochloric acid, which is accompanied by the production of a dye, takes place at a quite perceptible velocity. There are two points of inflection on the curve plotted from the pH values of the solution under titration.

The first point of inflection on this curve (Point A) represents the titration endpoint of the free sodium hydroxide in the solution, while the second (Point B) represents the titration endpoint of the diantipyrylphenylcarbinol. These findings indicate that titration of diantipyrylphenylcarbinol requires one equivalent of hydrochloric acid, the basicity constant of diantipyrylphenylcarbinol being $10^{-7.6}$.



Our observations have led us to conclude that the ionization of diantipyrylphenylcarbinol in an aqueous solution is accompanied by the splitting out of a hydroxyl ion and the constitution of a colored organic cation. Inspection of the structure of diantipyrylphenylcarbinol bears out the correctness of this conclusion.

In view of the fact that the properties of dyes containing antipyryl rings resemble those of the triphenylmethane dyes, it must be supposed that the carbinol compounds produced when triphenylmethane dyes are reacted with an alkali are likewise ionized similarly in aqueous solutions.

EXPERIMENTAL

In every experiment the solution pH was measured in a pH-meter using glass and calomel electrodes.

1. 0.0797 g of antipyryl orange was dissolved in 100 ml of water. The solution had a pH of 4.80 (temperature 17°).

2. 0.1124 g of diantipyrylphenylcarbinol was dissolved in 3.1 ml of 0.1N hydrochloric acid (T = 0.00363), the resultant solution being mixed with 193 ml of water. 3.5 ml of a 0.1N solution of sodium hydroxide (T = 0.00408) was added to the hydrochloric acid solution. The solution was gradually decolorized, the carbinol base remaining in solution. Back titration was commenced 2 hours later. After the next portion of hydrochloric acid had been added, readings were made every 4-5 minutes. The temperature of the solution under titration was 17° (Table 1).

TABLE 1

Ml of 0.1N HCl added	Galvanometer reading, millivolts	Ml of 0.1N HCl added	Galvanometer reading, millivolts
–	94	1.6	64
0.1	94	1.7	64
0.2	93	2.0	62
0.3	92	2.4	60
0.4	86	2.6	57
0.5	75	2.7	56
0.6	72	2.8	51
0.7	69	2.9	47
0.8	68	3.0	46
1.2	65	3.2	44
1.5	64	4.0	41

The titration curve is reproduced in the figure. Constitution of the dye required 2.3 ml of 0.1N hydrochloric acid (T = 0.00363). Calculation indicated that 2.3 ml of a carbinol solution with a pH of 8.9 was required; the pH of a solution constituting an equimolecular mixture of the dye and the carbinol was 6.6; the pH of the dye solution was 4.8. The basicity constant of diantipyrylphenylcarbinol, calculated from the pH at the point B, $K_B = 10^{-7.6}$.

3. 0.1542 g of antipyrine orange was dissolved in a mixture of 4 ml of a 0.1N solution of hydrochloric acid (T = 0.00358) and 196 ml of water, 8 ml of a 0.1N solution of sodium hydroxide (T = 0.00404) was added, and the mixture was set aside to stand. One hour later the solution of the carbinol base was back titrated with a 0.1N solution of hydrochloric acid. Readings were made 4-5 minutes after each portion of hydrochloric acid was added (Table 2).

TABLE 2

Ml of 0.1N HCl added	Galvanometer reading, millivolts
1.4	77
1.7	75
2.0	74
2.3	73
2.6	71
2.9	69

TABLE 3

Ml of 0.1N NaOH solution added	Galvanometer reading, millivolts	
	After the addition of NaOH	20 minutes later
–	69	–
0.3	93	72
0.6	93	73
0.9	93	74
1.2	93	76

After 2.9 ml of 0.1N hydrochloric acid had been added, back titration with 0.1N sodium hydroxide solution was commenced, the solution pH being read immediately after each portion of alkali had been added and then again 20 minutes later (Table 3).

SUMMARY

1. In aqueous solution the ionization of the carbinol compounds produced by the action of an alkali upon triphenylmethane dyes is accompanied by the splitting out of a hydroxyl ion and the formation of a colored organic cation.

2. The basicity constant of diantipyrylphenylcarbinol is $10^{-7.6}$ (17°).

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Received July 19, 1950

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THE PROBLEM OF THE SYNTHESIS OF β-HYDROXY ACIDS

SOME COMMENTS ON A.M. GAKHOKIDZE'S ARTICLES ON "CONDENSATION OF KETONES WITH ESTERS OF ORGANIC ACIDS"

N. F. Vulfson

No beta hydroxydicarboxylic acids have been known up to the present time. Kandiah [1] was unable to obtain the respective hydroxy acids even when he saponified the beta lactonic acids that are derivatives of malonic acid with alkalies. As we have shown, the rupture of the beta lactone ring in lactonic acids of this type by the action of alkali solutions is a first-order reaction and results in the formation of the tautomeric α, β-unsaturated dicarboxylic acids, rather than hydroxydicarboxylic acids [2]. In our study of the reaction in which beta lactonic acids are formed, we also found that although the derivatives of beta hydroxydicarboxylic acids are intermediate products of this process, they cannot be isolated because of their extreme instability [3]. That is why the brief paper by A. Gakhokidze and A. Guntsadze [4], in which they described the synthesis of β-hydroxyisopropylmalonic acid by condensing dimethyl malonate with acetone containing pulverized potassium hydroxide in the cold, awakened great interest on our part.

First, we should like to make some comments of a "formal" nature. The article by A. Gakhokidze and A. Guntsadze is exceptionally brief and laconic. The experimental information is confined to two sentences: "Two moles of acetone were used per mole of the ester" and "The reaction was carried out with chilling." Then the authors cite the constants of the dimethyl malonate they apparently employed, namely: b.p. at 20 mm, 131°; d_4^{20} 1.0384; n_D^{20} 1.4203, though the constants given in the literature for dimethyl malonate are: b.p. 70.3° at 11 mm and 73.0° at 13.5 mm, so that it cannot boil at 131° at 20 mm, but must have a b.p. that is 30° lower; d_4^{20} 1.1539 – 1.1544; n_D^{20} 1.41398 [5].

Then, after stating that two moles of acetone were used per mole of the ester, the authors write in their description of the experiment that "We took 160 g of the malonic acid ester for 116 g of acetone ..."; but 160 is the molecular weight of the diethyl ester, and not of the dimethyl ester. One might have thought that the constants cited above refer to the diethyl ester, i.e., the mention of the methyl ester was a misprint. But the constants do not even agree with those given in the literature for diethyl malonate: b.p. 73° at 6 mm, 88-89° at 13 mm, and according to our observations 102-103° at 26 mm; d_4^{20} 1.0550 – 1.0553; n_D^{20} 1.4128.

They state in the experimental section of their paper that the yield of the hydroxycarboxylic acid was 30% of the theoretical, while the figure given in their summary is 48%.

The authors give the constants of the diethyl ester of unsaturated isopropylidinemalonic acid as: b.p. 157° (10 mm); d_4^{20} 0.9945; n_D^{20} 1.4349. This substance has been repeatedly described in the literature [6] and has also been prepared by us; its constants are: b.p. 110-112° (10 mm); $d_4^{16.4}$ 1.0284; d_{25}^{25} 1.0254; n_D^{17} 1.44857; n_D^{25} 1.4478.

The analysis figures cited by the authors often differ from the calculated values by more than is allowable for experimental error (by 1.12%, for example for the silver salt of isopropylidenemalonic acid).

All that the authors say about the isolation of a new substance hitherto not described in the literature, a hydroxydicarboxylic acid, is: "49 grams of the acid were extracted ..."

Turning to the first report by A. Gakhokidze [7] on condensation of acetone with ethyl formate, ethyl acetate, and ethyl propionate, we learn that the author recommends boiling with a 10% alcoholic solution of potassium hydroxide to obtain the hydroxy acids. In this connection it is well to cite the observation of Koetz [8] that isopropylidenemalonic acid breaks down into acetone and malonic acid when it is agitated with aqueous ammonia, as well as our observation cited above, that the derivatives of beta hydroxydicarboxylic acids are so unstable that they cannot be isolated even under mild reaction conditions [3]. It is therefore highly unlikely that a hydroxydicarboxylic acid can be isolated by this method. This is also borne out by several observations made by M. M. Shemyakin and his associates on the hydrolytic cleavage of a double bond [9].

Having been working for a long time on analogous condensations and being greatly interested in the problem of whether beta hydroxydicarboxylic acids exist, we endeavored to repeat A. Gakhokidze's research. We observed a slight rise in temperature (to 8-12°) when diethyl malonate was reacted with anhydrous acetone and pulverized potassium hydroxide, chilled to 0° with absolute ether present. The precipitate gradually changed during the course of 2-3 hours, turning from a finely powdered one to a scaly form. No further changes were found. The reaction mass was set aside to stand for 2, 3, 10, and more days. Subsequent treatment, by the method recommended by A. Gakhokidze as well as by other methods, yielded nothing but the unchanged malonate and acid monoethyl ester of malonic acid. The scaly precipitate proved to be the potassium salt of this acid monoethyl malonate. A similar precipitate was secured when diethyl malonate was reacted with pulverized potassium hydroxide in absolute ether containing no acetone.

Nor did a repetition of the condensations with ethyl formate and ethyl acetate prove to be any more successful. We were unable to recover the respective beta hydroxy acids.

EXPERIMENTAL

Experiment 1. 116 g of anhydrous acetone and 160 g of diethyl malonate (the constants of which were exactly the same as those given in the literature) were dissolved in 200 ml of absolute ether chilled to 0°, and the solution was agitated while 50 g of finely powdered potassium hydroxide was added portionwise. The temperature of the reaction mass rose to 8-12°. Chilling was continued for 2 hours, after which the mass was set aside to stand at room temperature for 10 days (or 2, 3, 15 days, etc.), with agitation from time to time. Then the reaction mass was dissolved in water, the supernatant oil being removed and the aqueous layer washed with ether; the extract was combined with the removed layer, and the whole dried with sodium sulfate, after which the ether was driven off and the residue distilled in vacuo. This yielded 50 g of a distillate with a b.p. of 102-103° at 26 mm (98-99° at 23 mm); n_D^{24} 1.4115 (the diethyl ester of malonic acid). Saponification with alkali yielded malonic acid with an m.p. of 134-135°, which exhibited no depression of the melting point when mixed with an analytical sample.

Experiment 2. This reaction was similar. The precipitate was filtered out, washed with acetone, and dried. This yielded 100 g of scaly white crystals. The ether and acetone were driven out of the mother liquor, and the residue distilled in vacuo. This yielded 50 g of the malonic ester (see Experiment 1). The precipitate was dissolved in absolute methanol and saturated with anhydrous hydrogen chloride until no more precipitate was thrown down. The precipitate was filtered out, and the methanol driven off in a low vacuum. This left behind a light-yellow oil, which was water-soluble and was converted by heat into ethyl acetate, with a b.p. of 76-78°.

Analysis of the potassium salt: 0.0920, 0.1850 g substance: 0.0472, 0.0945 g K_2SO_4. Found %: K 22.93, 22.92. $C_5H_7O_4K$. Calculated %: K 22.93.

Experiment 3. 12.5 grams of pulverized potassium hydroxide was added portionwise, with agitation, to a solution of 40 g of diethyl malonate in 50 ml of absolute ether chilled to 0°. The subsequent processing and results were the same as those cited in Experiment 2.

We were unable to secure the corresponding hydroxy acids (hydroxyisobutyric and β-hydroxyisovaleric acid) by condensing acetone with ethyl formate and ethyl acetate in ether solution at 0° in the presence of pulverized potassium hydroxide.

SUMMARY

1. Repeating the A. Gakhokidze experiments on the synthesis of beta hydroxy acids does not bear out the results he describes.

2. The constants of the initial malonic ester cited in Gakhokidze's paper do not agree with the constants of diethyl or dimethyl malonate.

3. The constants of diethyl isopropylidenemalonate cited by the authors do not agree with those described for this substance.

4. The method of producing hydroxy acids proposed by Gakhokidze and Guntsadze, involving saponification by an alcoholic alkali, is inapplicable, owing to the ease with which these compounds are cleaved.

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Received November 29, 1948.

THE COMPOSITION AND INSTABILITY CONSTANTS OF SOME COORDINATION COMPOUNDS OF SILVER

M. B. Shchigol

Our previous reports [1-4] showed that the potentiometric titration of chlorides, iodates, bromates, oxalates and other salts in the presence of ammonia yields various coordination compounds with apparently different coordination numbers for silver (6, 4, 2). Thus, there are two saltuses on the titration curve (Fig. 1) when determining salts of monovalent anions. The first saltus occurs after half the silver nitrate has been added to the ammoniacal solution of the salt (if 5 ml of a 0.1 N solution of the salt were used, the first saltus would appear when 2.5 ml of 0.1 N $AgNO_3$ is added); the second saltus would appear on the curve after all the silver nitrate used in the reaction had been added (i.e., 5 ml of 0.1 N $AgNO_3$). Evidently, the first saltus represents the compound $[Ag(NH_3)_2X_2]^-$ (X representing a monovalent anion) with the coordination number 4 for silver, while the second saltus represents $[Ag(NH_3)_2]^+$ with the coordination number 2 for silver. When salts of divalent anions are titrated potentiometrically, there are three saltuses on the titration curve, the first apparently representing the complex ion $[Ag(NH_3)_2X_2]^{3-}$ with the coordination number 6 for silver (X being a divalent anion), the second representing $[Ag(NH_3)_2X]^-$ with the coordination number 4, and the third representing the complex ion $[Ag(NH_3)_2]^+$ with the silver coordination number 4.

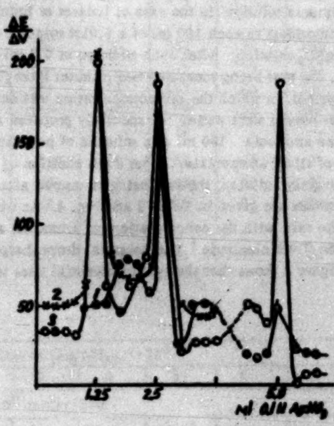

Fig. 1

1 - Titration of 5 ml of 0.1N NaCl solution in 10 ml of 1N ammonia solution; 2 - titration of 2.5 ml of 0.1 N KIO_3 solution in 10 ml of 0.1 N NH_3 solution; 3 - titration of 5 ml of K_2CrO_4 solution in 20 ml of 0.1N NH_3 solution.

The concentration of the complex ion diminishes as the ammonia concentration drops, for a constant salt concentration, the potential of the silver electrode increasing noticeably and the maximum rising at the points of equivalent saturation.

The latter circumstance proves that the ammonia and the salt anion are part of the inner sphere of the newly formed coordination compound, their proportions being identical, evidently. Studying the composition of these compounds is of distinct theoretical as well as practical interest by way of underpinning the previously developed method involving the potentiometric titration of various anions in ammonia.

As we know, there are various chemical and physicochemical methods used in studying the composition and the properties of coordination compounds. The most widely used of these methods are the potentiometric, polarographic, and optical methods. The work of various authors [5, 6, 7] has shown that optical research methods, particularly colorimetry, are wholly satisfactory in studying solutions of colored coordination compounds. The potentiometric and polarographic methods are best suited for research on uncolored coordination compounds. We have employed the potentiometric method for our ternary systems, comprising silver, ammonia, and salt ions.

If we consider the complex ion to be formed as follows:

$$Ag^+ + zNH_3 + zX^- \rightleftarrows [Ag(NH_3X)z]^-,$$

then

$$K = \frac{[Ag^+][NH_3]^z[X^-]^z}{[Ag(NH_3X)_z]^-}, \qquad (1)$$

i.e., when the concentration of the salt $[X^-]$ and of the ammonia or of either one of them in the solution is increased, the dissociation of the complex ion is repressed, and the concentration of free silver ions is diminished, resulting in a drop in the potential of the silver electrode. This is borne out experimentally.

The potential was measured with the usual potentiometric setup, a needle galvanometer with a sensitivity of 10^{-7} amp serving as a null instrument. The reference electrode was a saturated calomel electrode, a plate of pure silver serving as the indicator electrode. The test was run as follows: a) the potential of the system was measured for varying concentrations of the salt and constant concentrations of ammonia and silver nitrate; b) the system's potential was measured for a constant salt concentration and varying concentrations of the ammonia and silver nitrate. This was done by adding 10 ml of an 0.1N ammonia solution (in the case of iodates or bromates) or 10 ml of a 1N ammonia solution (in the case of chlorides) to each 100 ml of a 0.01N solution of the salt. The salt solutions were titrated with a 0.05N $AgNO_3$ solution. After each addition of 0.2 ml of silver nitrate solution, the solution was well agitated, the emf being measured two minutes later (Table 1, Figs. 2 and 3). For our research on the second system, in which the salt concentration was held constant, while the concentrations of ammonia and silver nitrate were varied, we specially prepared a 0.025N solution of silver ammoniate, containing 0.55N free ammonia. 100 ml of a solution of potassium iodate or bromate was titrated with a 0.025N solution of silver ammoniate. After each addition of 0.4 ml of the $[Ag(NH_3)_2]^+$ solution, the solution was thoroughly agitated, the emf being measured after the lapse of two minutes. The results of these measurements are given in Table 2 and Fig. 4. As we see from Fig. 2, an increase in the concentration of the salt, with the concentrations of ammonia and silver nitrate kept constant, lowers the potential of the silver electrode. The potential drops sharply at first, the drop slowing down somewhat thereafter. Figure 3 shows that the system potential rises with an increase in the concentration of silver ions, the concentrations of the salt and of the ammonia in the solution being kept constant. Figure 4 shows that raising the concentrations of the silver ions

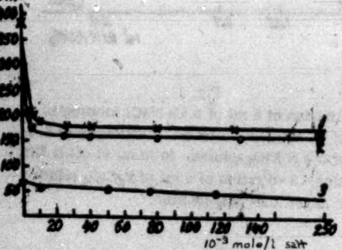

Fig. 2.

Change of potentials in a complex system as the salt concentrations are increased: BrO_3^- and IO_3^- ions in 10^{-2} mole of NH_3 per liter (Curves 1 and 2) and Cl^- in 10^{-1} mole of NH_3 per liter (Curve 3). $5.5 \cdot 10^{-4}$ mole of $AgNO_3$ per liter added.

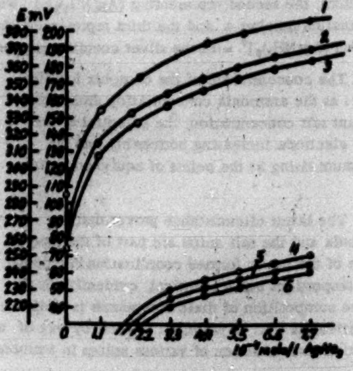

Fig. 3.

Change of potentials in a complex system when the salt and ammonia concentrations in the solution are held constant. Titration with an $AgNO_3$ solution: of water (Curve 1), of $0.5 \cdot 10^{-4}$ mole/liter IO_3^- (Curve 2), of $3.8 \cdot 10^{-4}$ mole/liter IO_3^- (Curve 3), of 10^{-2} mole/liter Cl^- (Curve 4), of $5 \cdot 10^{-2}$ mole/liter Cl^- (Curve 5), and of $7.5 \cdot 10^{-2}$ mole/liter Cl^- (Curve 6).

and the ammonia in the solution simultaneously, while the salt concentration is kept constant, lowers the potential of the silver electrode. All this is further proof of the formation of new coordination compounds in the solution.

TABLE 1

Composition of mixture, moles/liter		Moles per liter of $AgNO_3 \cdot 10^4$							
$C_{salt} \cdot 10^3$	$C_{NH_3} \cdot 10^3$	0	1.1	2.2	3.3	4.4	5.5	6.6	7.7
H_2O		E in millivolts, S.C.E.[1]							
100 ml	0	218	334	353	364	372	377	381	383
200 ml	1.0	77	147	168	179	188	193	199	204
$KBrO_3$									
0.587	1.0	74	141	159	171	180	188	193	198
1.13	1.0	74	140	156	169	178	184	187	194
3.4	1.0	76	135	153	164	173	180	185	193
25.00	1.0	78	125	143	156	166	174	179	185
KIO_3									
0.50	1.0	73	136	153	165	173	180	186	193
2.5	1.0	73	136	152	164	173	179	185	191
3.8	1.0	74	130	150	161	171	177	184	190
25.00	1.0	74	127	145	159	166	173	179	183
NaCl									
1.0	10.0	16	23	38	50	56	63	68	71
5.0	10.0	16	21	36	46	54	60	63	67
7.5	10.0	16	18	34	42	50	55	59	60
H_2O									
100 ml	10.0	16	36	51	61	70	75	79	85

TABLE 2

Composition of mixture, moles/liter	Moles per liter of $[Ag(NH_3)_2]^+ \cdot 10^4$							
	0	1	2	3	4	5	6	7
	$[NH_3] \cdot 10^3$ moles/liter							
	0	2.2	4.4	6.6	8.8	11.0	13.2	15.4
	E in millivolts, S.C.E.[1]							
100 ml H_2O	258	231	215	205	197	190	188	183
$KIO_3 \cdot 10^{-1}$	228	217	201	190	186	179	175	173
$KIO_3 \cdot 2.5 \cdot 10^{-1}$	212	201	190	182	175	171	167	164
$KBrO_3 \cdot 10^{-1}$	220	212	204	197	189	184	180	176
$KBrO_3 \cdot 2.5 \cdot 10^{-1}$	202	192	189	185	178	173	170	167

Determination of the Instability Constant and of the Number of Coordinated Groups

The data in Tables 1 and 2 may be used to calculate the instability constant of the complex ions and the number of coordinated groups. It follows from the equation for the instability constant (1) that

$$\frac{C_{Ag^+}}{C_{compl.}} = \frac{K}{(C_{NH_3} C_{X^-})^z}, \qquad (2)$$

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[1] S. C. E. = referred to saturated calomel electrode.

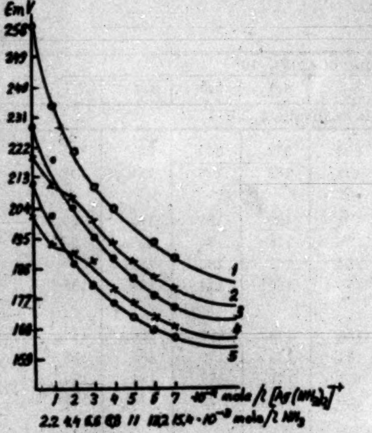

Fig. 4

Change of potentials in a complex system when the salt concentration is held constant and the concentration of ammonia in the solution is varied. Titration with an $AgNO_3$ solution: of water (Curve 1), of 10^{-1} mole/liter BrO_3^- (Curve 2), of $2.5 \cdot 10^{-1}$ mole/liter BrO_3^- (Curve 3), of 10^{-1} mole/liter IO_3^- (Curve 4), and of $2.5 \cdot 10^{-1}$ mole/liter IO_3^- (Curve 5).

where C_{Ag^+} is the concentration of silver ions (in gram-ions per liter); $C_{compl.}$ is the concentration of complex ions (in moles per liter); and C_X is the anion concentration, equalling the total salt concentration.

When the salt and ammonia concentrations are kept constant and the concentration of silver is varied, the ratio

$$\frac{C_{Ag^+}}{C_{compl.}}$$

will be a constant. Hence, the instability constant will depend upon the ratio between the concentration of silver ions and that of the complex ions, rather than upon their absolute values.

Rearranging Equation (2), we get

$$\frac{C_{compl.}K}{C_{Ag^+}} = (C_{NH_3}C_{X^-})^z. \qquad (3)$$

By comparing the value of the $C_{compl.}$ ratio at a given salt concentration and at various concentrations of ammonia and silver nitrate (A), we can readily find the value of the exponent z, i.e., the number of coordinated groups (Table 3). The concentration of free silver ions is found from the decrease in the potential of the silver electrode (Tables 1 and 2), as given by the formula:

$$E = E_0 - \frac{0.059}{n} \log \frac{A}{C_{Ag^+}}.$$

Thus, the mean value of z is nearly 2. We must take $[Ag(NH_3)_2X_2]^-$, as the formula for the complex anion, where X is a monovalent anion. Knowing

TABLE 3

	C_{salt}, moles per liter	C_{NH_3}, moles per liter	$C_{compl.}$, moles per liter	C_{Ag^+}, gram-ions per liter	$\log \frac{C_{compl.}}{C_{Ag^+}}$	z log $(NH_3 \cdot X)$	z
Cl^-	10^{-2}	10^{-1}	$5.5 \cdot 10^{-4}$	$2.7 \cdot 10^{-9}$	5.30	−3.00	
	10^{-2}	$2 \cdot 10^{-1}$	$5 \cdot 10^{-4}$	$7.7 \cdot 10^{-9}$	5.813	−2.70	1.71
	$4 \cdot 10^{-2}$	$4 \cdot 10^{-1}$	$100 \cdot 10^{-4}$	$5 \cdot 10^{-9}$	6.3	−1.80	
	$5 \cdot 10^{-2}$	10^{-1}	$7.7 \cdot 10^{-4}$	$3.44 \cdot 10^{-9}$	5.34	−2.30	1.92
BrO_3^-	$0.567 \cdot 10^{-2}$	$2 \cdot 10^{-2}$	$2.8 \cdot 10^{-3}$	$5.6 \cdot 10^{-7}$	3.70	−3.947	
	$0.567 \cdot 10^{-2}$	10^{-2}	$7.7 \cdot 10^{-4}$	$5.7 \cdot 10^{-7}$	3.13	−4.25	1.9
	10^{-1}	$0.44 \cdot 10^{-2}$	$2 \cdot 10^{-4}$	$7.3 \cdot 10^{-7}$	2.4	−3.36	
	10^{-1}	$0.88 \cdot 10^{-2}$	$4 \cdot 10^{-4}$	$4 \cdot 10^{-7}$	3.00	−3.06	2.00
IO_3^-	10^{-1}	$0.44 \cdot 10^{-2}$	$2 \cdot 10^{-4}$	$7.3 \cdot 10^{-7}$	2.4	−3.36	
	10^{-1}	$0.88 \cdot 10^{-2}$	$4 \cdot 10^{-4}$	$4 \cdot 10^{-7}$	3.00	−3.36	2.00
	$5 \cdot 10^{-3}$	10^{-2}	$7 \cdot 10^{-4}$	$5 \cdot 10^{-7}$	3.146	−4.30	
	$5 \cdot 10^{-3}$	$2 \cdot 10^{-2}$	$2.5 \cdot 10^{-4}$	$4.6 \cdot 10^{-7}$	3.736	−4.00	1.96

the value of z we can calculate the instability constant of the complex ion. Let the general formula for the complex ion be $[BX_2]^-$, where $B^+ = [AG(NH_3)_2]^+$; then $[BX_2]^- \rightleftharpoons BX + X^-$ and

$$K = \frac{[BX][X^-]}{[BX_2^-]} . \qquad (4)$$

Further dissociation of $BX \rightleftharpoons B^+ + X^-$, results in

$$K_{BX} = \frac{[B^+]^2}{[BX]}; \quad [BX] = \frac{[B^+]^2}{K_{BX}} . \qquad (5)$$

Inserting the value for [BX] in Equation (4), we get:

$$K = \frac{[B^+]^2 [X^-]}{A-B} . \qquad (6)$$

The concentration "B^+" is calculated from the potential drop in the system. Taking the potential measured when titrating 100 ml of a 0.01N ammonia solution (for IO_3^- and BrO_3^- ions) or 100 ml of a 0.1N ammonia solution (for Cl^- ions) with silver nitrate as E_0:

$$E = E_0 - \frac{0.059}{n} \log \frac{A}{B^+} .$$

The calculation of the instability constants is given in Tables 4, 5 and 6.

Thus, the mean value of the instability constant for complex ions, of the $[Ag(NH_3)_2X_2]^-$ type, where X is a monovalent anion, is $3 \cdot 10^{-5}$.

TABLE 4 Calculation of the Instability Constants for Complex $[Ag(NH_3)_2Cl_2]^-$

$C_{Cl^-} \cdot 10^3$ moles/liter	$C_{NH_3} \cdot 10$ moles/liter	E, V S. C. E.	E_0, V S. C. E.	$E_0 - E$, V S. C. E.	$C_{Ag^+} \cdot 10^5$ gram-ions/liter	$B^+ \cdot 10^4$ gram-ions/liter	$A \cdot 10^4$ moles/liter	$K \cdot 10^5$
1.0	1.0	0.063	0.377	0.314	2.63	3.47	5.5	0.8
5.0	1.0	0.060	0.377	0.317	2.34	3.00	5.5	1.8
7.5	1.0	0.050	0.377	0.322	1.90	2.50	5.5	1.87
1.0	1.0	0.071	0.383	0.312	3.86	4.40	7.7	0.52
5.0	1.0	0.067	0.383	0.316	3.44	3.85	7.7	1.92
7.5	1.0	0.060	0.383	0.323	2.60	2.90	7.7	1.31
1.0	2.0	0.085	0.428	0.343	7.70	25.00	50.00	2.50
5.7	3.0	0.064	0.428	0.364	7.0	20.00	100.00	2.85
							$K = 1.7 \cdot 10^{-5}$	

Relationship of the $[AgX_2]^-$ Constant to the Constant of the $[Ag(NH_3)_2X_2]^-$ Ion

As we know [8, 9], silver halides dissolve in an excess of halide salts, forming various coordination compounds. I. M. Korenman has calculated the instability constants for several coordination compounds of silver iodide, concluding that when silver iodide is dissolved in 0.3–1.9 moles of potassium iodide solution, the principal product is $K_3[AgI_4]$ ($K = 3.9 \cdot 10^{-15}$). Taking the figures given for the solubility of silver chloride [10] in solutions of sodium chloride, I. M. Korenman has found that silver chloride dissolves in solutions of up to 0.5 mole per liter of sodium chloride, forming the complex salt $K[AgCl_2](K[AgCl_2]^2 = 2.3 \cdot 10^{-4}$.

These findings enable us to establish the mathematical relationship between the instability constant of a complex ion of the $[AgX_2]^-$ type and the constant for a $[Ag(NH_3)_2X_2]^-$ ion. In effect, the compound $[Ag(NH_3)_2Cl_2]^-$ may be regarded as a product of the action of ammonia upon the $[AgCl_2]^-$ ion in accordance with the following equation: $[AgCl_2]^- + 2NH_3 \rightleftharpoons [Ag(NH_3)_2Cl_2]^-$, whence:

$$K = \frac{[AgCl_2^-][NH_3]^2}{[Ag(NH_3)_2Cl_2^-]} . \qquad (7)$$

Dissociation of the complex ion $[AgCl_2]^-$ yields: $[AgCl_2]^- \rightleftharpoons AgCl + Cl^-$, and:

$$K_1 = \frac{\text{"Pr"}\,[Cl^-]}{[AgCl_2^-]} = 2.3 \cdot 10^{-6}, \qquad (8)$$

whence

$$[AgCl_2]^- = \frac{\text{"Pr"}\,[Cl^-]}{2.3 \cdot 10^{-6}}. \qquad (9)$$

TABLE 5

Calculation of the Instability Constants for the Complex $[Ag(NH_3)_2(IO_3)_2]$

$C_{IO_3^-} \cdot 10^3$ moles/liter	$C_{NH_3} \cdot 10^2$ moles/liter	E, V S. C. E.	E_0,V S. C. E.	E_0-E, V S. C. E.	$C_{Ag^+} \cdot 10^7$ gram-ions/liter	$B^+ \cdot 10^4$ gram-ions/liter	$A \cdot 10^4$ moles/liter	$K \cdot 10^5$
10.00	1.0	0.179	0.372	0.193	2.6	3.0	5.00	4.5
25.00	1.0	0.173	0.372	0.199	2.3	2.3	5.00	5.20
3.8	1.0	0.191	0.379	0.188	4.4	4.2	7.00	2.39
10.00	1.0	0.191	0.379	0.188	4.4	4.2	7.00	6.30
25.00	1.0	0.183	0.379	0.196	3.3	3.2	7.00	6.60
0.5	2.0	0.192	0.413	0.221	4.6	1.7	25.00	1.80
10.00	0.66	0.190	0.205	0.015	–	1.7	3.00	2.23
10.00	0.88	0.186	0.197	0.011	4.0	3.4	4.00	3.7
10.00	1.1	0.179	0.190	0.011	–	3.1	5.00	3.4
10.00	1.32	0.175	0.186	0.011	–	3.8	6.00	6.5
25.00	0.66	0.182	0.205	0.023	–	1.2	3.0	2.0
25.00	0.88	0.175	0.197	0.022	–	1.7	4.0	3.2
25.00	1.1	0.171	0.190	0.023	–	2.4	5.0	5.76

Note. The instability constant of $[Ag(NH_3)_2(IO_3^-)_2]^-$ is estimated as $3.5 \cdot 10^{-5}$.

TABLE 6

Calculation of the Instability Constants for the Complex $[Ag(NH_3)_2(BrO_3)_2]^-$

$C_{BrO_3^-} \cdot 10^3$ moles/liter	$C_{NH_3} \cdot 10^3$ moles/liter	E, V S. C. E.	E_0, V S. C. E.	E_0-E, V S. C. E.	$C_{Ag^+} \cdot 10^7$ gram-ions/liter	$B^+ \cdot 10^4$ gram-ions/liter	$A \cdot 10^4$ moles/liter	$K \cdot 10^5$
3.4	1.0	0.173	0.372	0.199	1.9	2.5	4.4	1.12
25.00	1.0	0.166	0.372	0.206	1.46	1.87	4.4	3.50
0.567	1.0	0.198	0.383	0.185	5.7	6.68	7.7	2.54
3.4	1.0	0.193	0.383	0.190	4.6	5.07	7.7	3.15
0.567	2.0	0.195	0.413	0.218	5.6	21.0	28.0	3.57
10.00	0.44	0.204	0.215	0.011	7.3	1.26	2.0	2.00
10.00	0.66	0.197	0.205	0.008	–	2.2	3.0	6.00
25.00	0.66	0.185	0.205	0.020	–	1.4	3.0	1.90
25.0	0.88	0.178	0.197	0.019	–	1.9	4.0	4.30
25.00	1.10	0.173	0.190	0.017	–	2.5	5.0	6.25

Note. The instability constant of $[Ag(NH_3)_2(BrO_3)_2]^-$ may be taken as $3.44 \cdot 10^{-5}$.

The solubility product "Pr" of silver chloride is $1.69 \cdot 10^{-10}$, that of $[Cl]^-$ equaling the overall concentration of the salt. Inserting the $[AgCl_2]^-$ value in Equation (7), we get:

$$K = \frac{\text{"Pr"}\, C_{\text{salt}}\, C^2_{NH_3}}{2.3 \cdot 10^{-6}\, C_{\text{compl.}}}. \qquad (10)$$

The results of our calculation of K are given in Table 7.

TABLE 7

$C_{NaCl} \cdot 10^3$ moles/liter	a	C_{NH_3} moles/liter	$C_{compl.} \cdot 10^3$ moles/liter	$K \cdot 10^5$
4	0.9	0.4	1.0	4.22
5.7	0.89	0.3	1.0	3.36
7.5	0.87	0.1	0.077	6.6
4.0	0.90	0.4	2.0	2.16
				$K = 4 \cdot 10^{-5}$

TABLE 8

C_{KIO_3} moles/liter	a	$[IO_3^-] \cdot 10^3$ gram-ions/liter	Solubility of $AgIO_3 \cdot 10^5$, moles/liter	$K_1 \cdot 10^6$
0.005	0.960	4.8	6.0	3.15
0.025	0.920	23.00	50.00	1.61
0.50	0.900	45.0	83.0	1.90
				$K_1 = 2.22 \cdot 10^{-6}$

The literature does not give the values of the instability constants for other complex silver ions, such as $[Ag(IO_3)_2]^-$. Hence, calculation of the instability constant of the complex ion $[Ag(IO_3)_2]^-$ required the preliminary study of the solubility of silver iodate in solutions of potassium iodate. These tests were run as follows: Precipitates of silver iodate were transferred to 100-ml measuring flasks, 25 ml of distilled water was added, and given amounts of potassium iodate were introduced. The total volume was raised to 100 ml by adding water, the solution was agitated for 24 hours, and then it was filtered, the iodate in the filtrate being determined iodometrically. The temperature ranged from 20-22° in the various test series.

The calculation was made as follows: the solubility $\underline{P}$ of silver iodide in a potassium iodide solution may be expressed as:

$$P = [Ag^+] + [Ag(IO_3)_2]^- = \frac{\text{"Pr"}}{[IO_3^-]} + [Ag(IO_3)_2]^- . \quad (11)$$

Allowing for dissociation of the complex ion $[Ag(IO_3)_2]^-$ and substituting the appropriate value of the $[Ag(IO_3)_2]^-$ concentration in Equation (11) we find that:

$$P = \frac{\text{"Pr"}}{[IO_3^-]} + \frac{\text{"Pr"}\,[IO_3^-]}{K_1}, \text{ whence} \qquad K_1 = \frac{\text{"Pr"}\,[IO_3^-]a}{P - \frac{\text{"Pr"}}{[IO_3^-]}} . \quad (12)$$

The means of three determinations are listed in Table 8.

Substituting the values found for $\underline{K_1}$ and "Pr", $K_1 = 2.22 \cdot 10^{-6}$ and "Pr" $= 3.5 \cdot 10^{-8}$, in Equation (10), we can compute the constant for $[Ag(NH_3)_2(IO_3)_2]^-$. We find the mean value of the instability constant of the $[Ag(NH_3)_2(IO_3)_2]^-$ ion to be $2 \cdot 10^{-5}$.

Thus, the instability constants of the new coordination compounds, determined potentiometrically and computed from the constants for silver coordination compounds of the $[AgX_2]^-$ type, are of the same order of magnitude, $\underline{K} = 3 \cdot 10^{-5}$.

Some Theoretical Considerations

The results of research on ternary systems consisting of $AgNO_3 - NH_3 -$ alkali metal halides and other salts convincingly prove that coordination compounds with the general formula of $[Ag(NH_3)_2X_2]^-$, in which the inner sphere of the complex ion contains two ammonia groups in addition to the salt anion, are formed in the solution. We thus get mixed coordination compounds that are fairly stable in solutions containing an excess of ammonia and cannot be isolated in the crystalline state. As Ya. A. Fialkov [11] has said, the inability to isolate a coordination compound from the solutions by crystallization is no proof that there is no such compound in the solution. It must therefore be assumed that the complex salt in solution has a different composition from the coordination compound that could be secured by means of crystallization.

The problem of the connection between the valence of the element and its coordination number is of some interest in view of the fact that mixed coordination compounds of the $[Ag(NH_3)_2X_2]^-$ type, in which the coordination number of the silver is 4 and 2, or 6, 4 and 2 in the case of divalent ions (instead of the coordination number of 2 adopted for silver), are formed in the $AgNO_3 - NH_3 - MeX$ ternary systems.

Grinberg [12], for instance, believes, quite justly, that elements with varying valence should exhibit coordinating ability. Therefore, we must speak of the coordination number of divalent platinum, tetravalent platinum, monovalent copper, divalent copper, and so forth. It is quite clear that the coordination number is a variable and that a given element is able to exhibit different coordination numbers in different compounds, even when its valence is constant. This circumstance is closely bound up with the conditions under which the coordination compound is produced, with the nature of the reacting ions and coordinated groups, and with other factors as well, such as temperature and pressure.

A number of coordination compounds of silver are known, such as silver ammoniates, silver chlorides, silver cyanides, and the like [13], in which the silver coordination numbers are 1, 2, 3, or 4. Hence, it is quite possible to secure coordination compounds in solution that have several coordination numbers, even for elements with constant valence. We have confirmed this. The basic valence of silver in these compounds remains one, in contrast to the other known silver compounds with a coordination number of 4: $[AgPy_4]^{2+}$, $[AgPhn_2]^{2+}$, 1) in which the silver has a basic valence of 2. As we know, these latter compounds are noted for their high oxidizing ability [14].

The compounds of the $[Ag(NH_3)_2X_2]^-$ ion type that we have synthesized are not oxidants. They must be regarded simply as saturated coordination compounds, whereas the $[Ag(NH_3)_2]^+$, $[AgPy_4]^{2+}$, and other complex ions are unsaturated coordination compounds. One cannot, of course, speak of the identical stability of coordination compounds with a variable coordination number for the central atom. Obviously the compounds in which the central atom exhibits its "normal" coordination number will be most stable. For instance, $[Ag(NH_3)_2]^+$ $(K = 6.8 \cdot 10^{-8})$ is more stable than the complex ion $[Ag(NH_3)_2X_2]^-$ $(K = 3 \cdot 10^{-8})$.

The ions of divalent copper exhibit the coordination numbers 3, 4, and 6, the most stable copper compounds being those with coordination numbers of 3 and 4 for the copper, and those with a coordination number of 6 being least stable. The coordination numbers of zinc and nickel are 6, 4, and 3, the most stable compounds being those with a coordination number of 6, and the least stable those in which the coordination numbers of the zinc or nickel are 4 and 3, and so forth. This is possibly due to the difficulty of securing certain coordination compounds in the free state (different stability of the complex salt in solution and in the solid state).

SUMMARY

1. It has been proved that a mixed complex ion of the $[Ag(NH_3)_2X_2]^-$ type, with the silver having a coordination number of 4, exists in solution.

2. The number of coordinated groups and ions within the inner sphere of the complex ion has been calculated, as well as the instability constants for various complex silver salts.

3. The mean value of the instability constant of a complex ion of the $[Ag(NH_3)_2X_2]^-$ type has been found to be $3 \cdot 10^{-8}$ (X being a monovalent anion).

4. The suggestion is advanced that elements with constant valence, as well as elements with variable valence, may form coordination compounds of the mixed type with different coordination numbers for the central ion. The appearance of elements with differing coordination ability is directly related to the conditions under which the coordination compounds are produced, as well as to the nature of the reacting ions.

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Received July 11, 1950

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1) Phn denotes phenanthroline.

SPECTROPHOTOMETRIC INVESTIGATION OF THE INTERACTION OF HALIDES DISSOLVED IN CCl_4

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That halides can react with one another has been known for a long time. Gay-Lussac [1], for example, established the existence of compounds of I_2 and Cl_2, while Balard [2, 3] did the same for I_2 and Br_2, Br_2 and Cl_2, etc. Interest in these compounds has continued down to the present, because they are of theoretical as well as practical importance. Doubts have often been expressed, however, concerning the existence of many of these compounds, particularly IBr and BrCl [4, 5, 6] (probably owing to their slight stability [7]). The methods of producing these compounds as well as their refining, are extremely laborious, so that the properties of BrCl, say, are not sufficiently known even now, while IBr forms mixed crystals with the initial components [6] and decomposes during purification. Several papers have been written on the solutions of these compounds. These papers have established the effect of the solvent upon the formation and the behavior of these compounds in solution [22]. We find numerous contradictions in some papers dealing with such thoroughly investigated compounds as ICl. In the older papers [8], for example, we find that when ICl is dissolved in CCl_4, it decomposes as follows: $3ICl \rightarrow I_2 + ICl_3$. Papers published somewhat later, however, state that ICl_3 does not exist at all in CCl_4, breaking down as follows: $ICl_3 \rightarrow ICl + Cl_2$ [9]. Analogous contradictions are to be found in papers dealing with IBr [9, 10].

The direct production of interhalogen compounds in solution, especially in carbon tetrachloride as a "neutral" solvent, should be of particular interest in research into the effect of the solvent upon such compounds [11].

The researches of Gillam and Morton [9] and of Barrat and Stein [12] on such solutions suffer from various deficiencies. The identity of the spectra of solutions of ICl and IBr in CCl_4, prepared by dissolving the previously produced compounds or by directly mixing together equivalent proportions of the respective halides, for instance, is not sufficient proof of the formation of the compounds ICl and IBr in solutions.

The paper on BrCl [12] contains several propositions that must be criticized.

The use of physicochemical analysis in resolving the problem of the interaction of halogens ought to yield more definite results. We have chosen one of the variants of this method, the tested property being the optical density, measured with a spectrophotometer.

We employed the so-called method of "continuous variations" [14, 15, 16], as it is now more and more widely used in the investigation of reactions occurring in solutions [17-21]. Together with the investigation of such systems as ICl, in which the presence of a compound may be felt to be doubtful, our paper serves as further proof of the applicability of the method itself, which, like many another method of physico-chemical analysis, requires careful checking [13]. The method has been described in various papers [14, 15], so that we shall deal with it only briefly.

The Method of Continuous Variations

This method is based upon the determination of a singular point in the function: $y = d_C - d_{X_I} - d_{X_{II}}$ (provided ΣM = constant, i.e., the sum of the component concentrations in the mixed solutions must remain constant);

d_C is the optical density of the solution prepared by mixing together Solution I, containing v ml of halogen X_I and Solution II, containing $(1 - v)$ ml of halogen X_{II}; d_{X_I} and $d_{X_{II}}$ are the optical densities of the pure components in concentrations corresponding to those in the given mixture.

We prepared 9 solutions of equimolecular concentration, the total volume being either 10 or 5 ml.

EXPERIMENTAL

Particular care was taken with the purification of the reagents. The CCl_4 was thoroughly purified, with chief stress laid on eliminating the CS_2. The check was made spectrophotometrically to within 0.002% [33]. We used the Schuwitz-Dumon method of purifying the CCl_4 [24]. The check included measurement of the refractive index. We found that additional chlorination of the CCl_4 with I_2 present as a catalyst successfully removed the $\lambda = 318$ mμ absorption line. Great care was also paid to drying, for the slightest trace of water would cause turbidity when the halogens were added, especially when the constitutent reagents were mixed together. Dying was effected with $CaCl_2$, P_2O_5, and distillation over metallic sodium. Distillation was performed in a flask with a neck 75 cm long and at a constant temperature of 76.5°. The (chemically pure) I_2 was refined by double slow subliming from a mixture with KI [25].

The bromine was purified by the D. I. Mendeleev method [26] and distilled by the Honigschmidt and Zintley method [26].

The chlorine was prepared from MnO_2 and HCl and was dried in a drying battery containing $CaCl_2$ and H_2SO_4.

The solutions of the initial substances were always made immediately prior to their mixing, in order to avoid all outside influences.

The concentrations of the halogens in the solutionwere determined by titration [28, 29, 30] as well as spectrophotometrically.

The chlorine solution used in preparing the mixtures was taken from a bottle directly connected to a buret; as the buret was filled, air entered the bottle only via another vessel containing a solution of Cl_2 in CCl_4 of the same concentration (this eliminated any error due to a change in the concentration of the chlorine solution).

The reaction lasted some time (the spectra changing), so that we kept the components in sealed ampoules to prevent the evaporation of the components or the compounds (the ampoules were filled at a temperature below the melting point of CCl_4 and opened just before measurement).

As a rule, 12 to 20 hours elapsed between the preparation of the solutions and the measurements.

A Beckmann quartz spectrophotometer (Model D. U.) was used in our measurements [23]. The glass cells, 10, 5, and 2.5 mm long, could not be closed tightly, so that measurements were made at only a few wavelengths (lasting 3-5 minutes).

Our first problem was measuring the spectra of halogens dissolved in CCl_4.

1) Absorption Spectrum of a Chlorine Solution

Despite all the precautions we had taken in preparing the chlorine solutions we took two simultaneous sample to avoid any errors due to changes in concentration: one in a cell for spectral measurements, and the other for quantitative analysis. Measurements were made quickly and were repeated several times, the mean of several measurements being taken as the final result.

We found agreement with the Lambert-Beer law within the following concentration range: 0.01-0.06 mole/liter, and in the following spectrum range: $\lambda = 270 - 460$ mμ. This enabled us to compute the molar absorption coefficients, which are listed in Table 1.

In the paper by Gillam and Morton [9] cited above we find the absorption maximum for Cl_2 at $\lambda = 332$ mμ and the coefficient to be 99.

In the paper by Barrat and Stein [12] we see from a curve that the absorption maximum is at about $\lambda \parallel 330$ mμ, with the coefficient about 80. The difference is probably due chiefly to evaporation of the chlorine.

2) Absorption Spectrum of a Bromine Solution

Conformity with the Lambert-Beer law has been found to exist at concentrations of 0.005-0.06 mole/liter and in the 330-625 mμ spectrum region [12, 31]. The results of our calculations of the molar absorption coefficient are listed in Table 2.

TABLE 1

λ	ε	λ	ε	λ	ε
460	1.30	350	73.8	310	62.8
420	3.4	340	89.6	300	38.1
400	7.3	334	94.5	290	19.5
380	21.7	330	93.5	280	7.7
370	35	326	92.5	270	3.7
360	53.6	320	82.8	–	–

TABLE 2

λ	ε	λ	ε	λ	ε
625	2.6	480	122.5	360	32.7
600	4.7	460	147	340	5.5
580	9.9	440	180.5	330	2.6
560	19.6	420	213	320	2.5
540	36.7	400	186	300	2.7

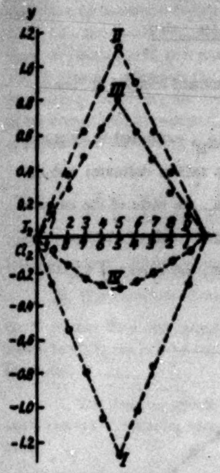

Fig. 1. System I_2-Cl_2.

ΣM = 0.045 mole/liter
I) λ = 580 mμ ; II) λ = 440 mμ ; III) λ = 400 mμ ; IV) λ = 360 mμ ; (cell length l = 2.5 mm).

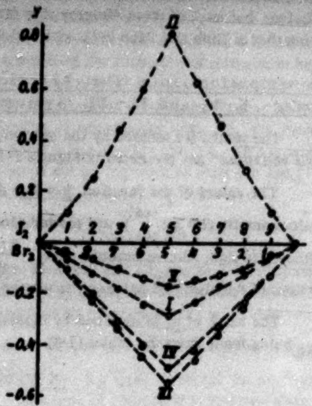

Fig. 2. System I_2-Br_2. ΣM = 0.0105 mole/liter. I) λ = 600 mμ ; II) λ = 440 mμ ; III) λ = 400 mμ ; IV) λ = 380 mμ ; V) λ = 360 mμ ; cell length l = 10 mm).

3) Absorption Spectrums in Iodine Solutions

Conformity with the Lambert-Beer law has been found to exist at concentrations of 0.0005-0.045 mole/liter and in the spectrum region of λ = 750-380 mμ , the law no longer applying at the shorter wavelengths [27]. Our results are for the concentration of 0.001 mole per liter. These results are presented in Table 3 and Figure 3.

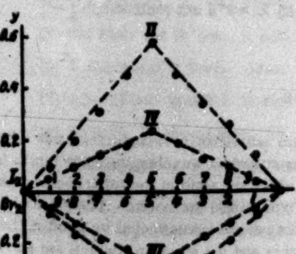

Fig. 3. System I_2-Br_2. ΣM = 0.005 mole/liter. I) λ = 580 mμ ; II) λ = 460 mμ ; III) λ = 400 mμ ; IV) λ = 300 mμ (cell length l = 10 mm).

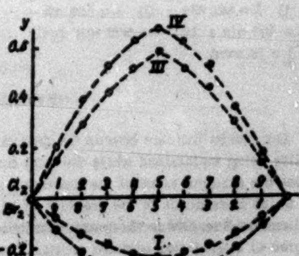

Fig. 4. System Br_2-Cl_2. ΣM = 0.06 mole/liter. I) λ = 520 mμ ; II) λ = 500 mμ ; III) λ = 380 mμ ; IV) λ = 370 mμ ; (cell length l = 2.5 mm).

TABLE 3

λ	ε	λ	ε	λ	ε
750	12	490	724	390	8
700	35	480	568	380	12
650	51	470	328	370	13
600	121	460	234	360	14
580	254	450	164	340	21
550	629	440	92	330	22
540	722	430	49	320	30
530	886	420	25	300	48
520	946	410	14	–	–
500	857	400	10	–	–

There are various references in the literature to the absorption of iodine solutions, but most of them disagree, the most dependable of all the researches being that of Groh and Papp [27], with which our results agree in the main.

Investigation into the Reactions in the I_2-Cl_2; I_2-Br_2 and Br_2-Cl_2 Systems

The results we secured by the spectrophotometric method of "continuous variations" are presented in Figures 1-6.

The values of the function $\underline{y} = d_c - d_{X_I} - d_{X_{II}}$, expressed in units of optical density ($I = I_0 c^{-\varepsilon d l}$), are plotted along the axis of ordinates with the appropriate sign; the volumetric ratio $\frac{1-v}{v}$ i.e., the ratio of the concentrations of the dissolved halogens, is plotted along the axis of abscissas.

The value of $\underline{d_c}$ is obtained by measurement, the values of d_{X_I} and $d_{X_{II}}$ being found from the tables (1-3).

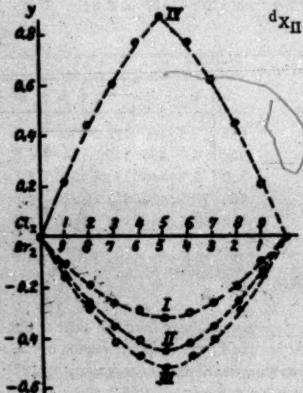

Fig. 5. System Br_2-Cl_2. $\Sigma M = 0.02$ mole/liter. I) λ = 520 mμ ; II) λ = 500 mμ ; III) λ = 480 mμ ; IV) λ = 370 mμ (cell length $\underline{l}$ = 10 mm).

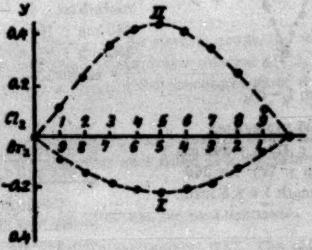

Fig. 6. System Br_2-Cl_2. $\Sigma M = 0.01$ mole/liter. I) λ = mμ ; II) λ = 370 mμ (cell length $\underline{l}$ = 10 mm).

EVALUATION OF RESULTS

Our results indicate beyond the shadow of a doubt that the results are satisfactorily reproducible, this reproducibility being maintained while the total concentration varies, as well as at various wavelengths. The results indicate that the extreme value of the function $\underline{y}$ occurs at a composition for which the ratio of the initial components is 1:1, which is evidence of the presence of a compound of the $(X_I \cdot X_{II})_n$ type within the system. The applicability of the Lambert-Beer law to these solutions indicates that the number of color centers is unaffected by dilution (i.e., the degree of dissociation remains constant, inasmuch as the initial substances and the reaction products are all colored) [32]. We know that the degree of dissociation may remain practically constant during dilution either when the dissolved compound is very stable or when dissociation is not accompanied by a change in the number of molecules.

Thermodynamical data and various other considerations exclude the first hypothesis, so that we must picture the reaction as follows:

$$(X_I)_2 + (X_{II})_2 \rightleftarrows 2X_I \cdot X_{II},$$

i.e., of all the possible $\underline{n}$ polymers, only $X_I \cdot X_{II}$ actually exists.

Notwithstanding certain fluctuations of the results toward one side or the other, due to evaporation of the components or to purely experimental errors in measurement, all our curves exhibit the complete symmetry of the function to the right and left of the experimental point. It is not difficult to show, by analysis of the function $\underline{y}$, that this circumstance is one of the proofs of the existence of interaction between the components only in a 1:1 ratio, i.e., the results indicate that no other type of compounds absorbing light in other regions of the spectrum than those we investigated can exist under the specified conditions. It may be added that the extreme points of the ICl and IBr systems represent the intersection of two straight lines, i.e., the extreme point is sharply demarcated. In the BrCl system, however, the extreme point is less sharply marked. This is probably caused by the differing stability of the compounds mentioned, as is borne out by the work of Blair and Jost [7], who give $a = 0.25\%$ as the degree of dissociation for ICl, $a = 0.5\%$ for IBr, and $a = 52.4\%$ for BrCl.

SUMMARY

1. The interaction of halogens dissolved in CCl_4 has been investigated spectrophotometrically for the first time, using the method of "continuous variations", the applicability of this method to instances where the kind of interaction had already been established by other methods also having been checked.

2. The location of the extreme point as well as the symmetry of the function $\underline{y} = \underline{d}_C - d_{X_{II}} - d_{X_{II}}$, leads us to conclude that only one compound, of the $X_I \cdot X_{II}$ type, exists (at the concentrations given) when two halogens dissolved in CCl_4 are mixed together. This type of compound is retained even when one of the components is present in excess.

3. The results, which indicate the presence of compounds of I_2 and Br_2, dissolved in carbon tetrachloride, again remove the doubts that have arisen in the minds of some authors as to the possibility of any such interaction at all.

4. The presence of the compound BrCl in CCl_4 solutions has been convincingly proved for the first time.

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Received September 26, 1950

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THE LAWS GOVERNING CHANGE IN SOLUBILITY

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As we have shown in our preceding paper [5], the following laws hold good for the Raoult coefficient r in a binary system, found from the equation:

$$r = \frac{C}{P_0 - \pi} \quad (1)$$

where P_0 and π are the saturated vapor pressure above the pure solvent and above a solution of concentration C, respectively, for a constant quantity of solvent:

1) For isotherms:

$$r = r_0 + \rho C, \quad (2)$$

where r_0 and ρ are constants.

2) For polytherms:

a) For unsaturated solutions of constant concentration:

$$r = \exp\left(\frac{a}{T} + b\right), \quad (3)$$

b) For saturated solutions.

$$r = \exp\left(\frac{A}{T} + B\right), \quad (4)$$

where a, b, A, and B are constants.

In the present paper which represents a continuation of our previous researches [1,2,3,4,5], we shall discuss the conclusions that stem from deviations from Raoult's law.

Isothermal deviations from Raoult's law for unsaturated solutions in multicomponent systems. We may regard an unsaturated solution of constant concentration as a new solvent, to which all the general laws governing solutions in the binary systems: solvent—solute apply [3].

Equation (2) indicates that the magnitude of the Raoult coefficient changes in binary systems. By analogy we may then write for unsaturated solutions in multicomponent systems:

$$\bar{r} = \bar{r}_0 + \bar{\rho}C, \quad (5)$$

where the symbols with lines over them denote the respective values of the variables in the new solvent, and C is the concentration of the component with which the solution is saturated.

By way of example illustrating the correctness of Equation (5), we cite the data in the ternary system $NaCl-C_{12}H_{22}O_{11}-H_2O$ at 25° [6] for the solubility of $C_{12}H_{22}O_{11}$ (C_2) in $NaCl-H_2O$ solutions in which the NaCl concentration is approximately constant ($C_1 \approx$ const.).

As the experimental findings indicate (Table 1, Figure 1), the Raoult coefficient $\bar{r}$ calculated from Equation (1) is a linear function of the concentration of the variable component C_2 dissolved in a complex solvent ($NaCl-H_2O$):

$$\bar{r} = \bar{r}_0 + \bar{\rho}C_2,$$

thus confirming Equation (5).

Isothermal change of pressure in saturated solvent vapors. It follows from Equations (1) and (2) that:

$$\pi = P_0 - \frac{C}{r_0 + \rho C}, \quad (6)$$

i.e., saturated vapor pressure of the solvent above the solution is a hyperbolic function of the solution concentration expressed for a constant quantity of the solvent.

Rearranging Equation (6), we get:

$$\frac{1}{P_0 - \pi} = \frac{r_0}{C} + \rho, \tag{7}$$

whence it follows that there is a linear relationship between the reciprocals of the drop in pressure and of the solution concentrations as expressed for a constant quantity of the solvent.

We cite the data for the $K_2SO_4-H_2O$ and $NaI-H_2O$ systems as examples illustrating the correctness of Equation (7).

The figures for the $K_2SO_4-H_2O$ system at 30 and 80° [7] are given in Tables 2 and 3 and plotted in Figures 2 and 3 respectively.

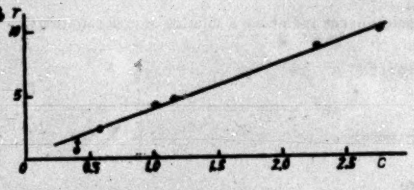

Fig. 1. $NaCl-C_{12}H_{22}O_{11}-H_2O$; 25° isotherm $NaCl:C_1$ = const.

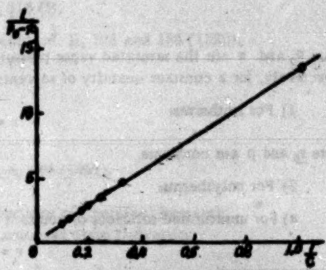

Fig. 2. $K_2SO_4-H_2O$; 30° isotherm.

The figures for the $NaI-H_2O$ system at 100° [8] are given in Table 4 and plotted in Figure 4.

In these figures the values of the reciprocal concentrations are plotted along the axis of abscissas, with the values of the reciprocal pressure drops of the saturated vapor pressure of the solvent above the solution plotted as ordinates. We see from Figures 2, 3, and 4 that the function is actually linear, i.e., Equation (7) holds.

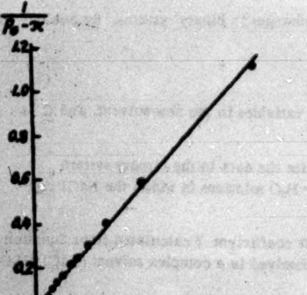

Fig. 3. $K_2SO_4-H_2O$; 80° isotherm.

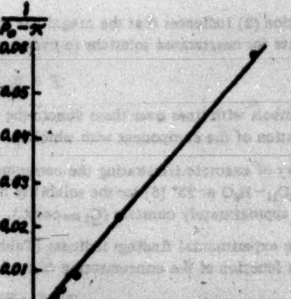

Fig. 4. $NaI-H_2O$; 100° isotherm.

SUMMARY

1. It has been shown that the change in the value of the Raoult coefficient for solutions of a substance dissolved in an unsaturated solution in which the concentration of the other components is constant obeys the same

TABLE 1

$NaCl-C_{12}H_{22}O_{11}-H_2O$ (6) 25° isotherm

Solution composition in moles/1000 g. H_2O		$\frac{P_0}{\pi}$	$\frac{\pi}{P_0}$	$\frac{P_0-\pi}{P_0}$	$P_0 \cdot r$
NaCl C_1	$C_{12}H_{22}O_{11}$ C_2				
6.22	0.40	1.338	0.7474	0.2526	1.584
6.23	0.58	1.340	0.7463	0.2537	2.287
6.33	1.03	1.349	0.7413	0.2587	3.975
6.33	1.18	1.352	0.7396	0.2604	4.531
6.54	2.34	1.388	0.7205	0.2795	8.371
6.63	2.82	1.405	0.7117	0.2883	9.779

TABLE 2

$K_2SO_4-H_2O$ (7) 30° isotherm

C g/100 g H_2O	π (mm Hg)	$P_0-\pi$ (mm Hg)	$\frac{1}{C}$	$\frac{1}{P_0-\pi}$
0	31.834	0	–	–
1	31.76	0.07	1.000	14.29
2	31.68	0.15	0.500	6.667
3	31.62	0.21	0.333	4.762
4	31.55	0.28	0.250	3.571
5	31.49	0.34	0.200	2.941
6	31.43	0.40	0.167	2.500
8	31.30	0.53	0.125	1.887
10	31.18	0.65	0.100	1.538

TABLE 3

$K_2SO_4-H_2O$ (7) 80° isotherm

C g/100 g H_2O	π (mm Hg)	$P_0-\pi$ (mm Hg)	$\frac{1}{C}$	$\frac{1}{P_0-\pi}$
0	355.47	0	–	–
1	354.6	0.9	1.000	1.1111
2	353.8	1.7	0.500	0.5882
3	353.0	2.5	0.333	0.4000
4	352.3	3.2	0.250	0.3125
5	351.6	3.9	0.200	0.2564
6	350.9	4.6	0.167	0.2174
8	349.6	5.9	0.125	0.1695
10	348.2	7.3	0.100	0.1370
15	344.7	10.8	0.067	0.0926
20	341.2	14.3	0.050	0.0699

TABLE 4

$NaI-H_2O$ (8) 100° isotherm

C g/100 g H_2O	π (mm Hg)	$P_0-\pi$ (mm Hg)	$\frac{1}{C}$	$\frac{1}{P_0-\pi}$
0	760	0	–	–
10	743	17	0.10000	0.058823
25	715	45	0.04000	0.022222
50	652	108	0.02000	0.009259
75	581	179	0.01333	0.005587
100	511	249	0.01000	0.004016
125	443.5	316.5	0.00800	0.003160
150	383.5	376.5	0.00667	0.002656
175	332	428	0.00571	0.002336
200	288	472	0.00500	0.002119
225	251.5	508.5	0.00444	0.001967
250	221	539	0.00400	0.001855
275	195.2	564.8	0.00364	0.001770
300	173.3	586.7	0.00333	0.001704

laws that hold for binary systems of a solute and a pure solvent.

2. It has been shown that there is a linear relationship between the reciprocals of the drops in pressure and solution concentrations, expressed for a constant quantity of solvent.

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Received February 18, 1951.

ELECTRODE POLARIZATION IN THE ELECTROLYSIS OF NICKEL AND COBALT AT A DROPPING MERCURY CATHODE. I.

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In the securing of reproducible, sharply distinct, volt-ampere curves for the electrolysis of metals, especially nickel and cobalt (using a dropping mercury cathode), the properties of the "indifferent" electrolyte in which the polarographic process takes place are of great importance. These properties determine the nature of the polarographic waves, their form and height, the occurrence of maxima, etc. There is no universal polarographic medium, since its choice is frequently dictated by the composition of the substance under test and by the entire setup of the investigation [1].

Nickel and cobalt, elements whose chemical properties are very similar, are deposited at the same potential upon a platinum electrode. The polarographic method enables one to separate their deposition zones by selecting a suitable "indifferent" electrolyte.

Establishing the nature and magnitude of the electrode polarization occurring during the electrolysis of nickel and cobalt in an ammoniacal medium, investigating the influence of oxalate, tartrate, citrate, and salicylate media upon electrode polarization, and investigating the behavior of the ions of these metals in the presence of thiourea, urotropine, and potassium thiocyanate and the influence of these substances upon the nature of the diffusion waves are of considerable interest in selecting the optimum conditions, which make it possible to electrolyze nickel and cobalt together. Research into these problems is the objective of the present paper.

Theoretically, a certain potential $\underline{E}$ must be applied in electrolysis for a metal to begin to be deposited upon the cathode:

$$E = E_0 + \frac{RT}{nF} \ln C. \tag{1}$$

In practice $\underline{E}$ often exceeds $\underline{E_0}$, the theoretically calculated value, quite considerably. Concentration polarization is very small, usually not exceeding hundredths of a volt [2]. No research has as yet been done on chemical polarization, which greatly affects the electrolysis of nickel and cobalt. Its value often totals hundredths and even tenths of a volt [3].

As we know, the electrolysis of metals consists of several successive stages: the retardation of any one of them may interfere with the securing of an electrochemical reaction product and cause further polarization. At the present time the theory of retarded ion discharge, developed in the Soviet Union by Izgaryshev, Frumkin, and others, must be regarded as the most probable. When metals are electrodeposited on a platinum cathode, chemical polarization may also be caused by a retardation in the rate at which crystal nuclei arise during the formation of the crystal lattice [4,5]. This factor is eliminated when we employ a dropping mercury electrode. The continuous renewal of the mercury surface completely eliminates the effect of any previous processes, while the concentration of the reduced nickel and cobalt ions is so low during polarography that the formation of an amalgam cannot cause chemical polarization, so that the latter must be attributed to action occurring within the solution, i.e., the retarded decomposition of the complex metal ions.

If the ions of the principal electrolyte (the medium) do not react with certain ions, the nature of the principal electrolyte and its concentration (within certain limits: 0.01-0.10 N) have practically no effect upon $E_{1/2}$, since the ionic strength of the solution must be high enough to produce a perceptible deviation of the half-wave potential. Its shift in the given case may be elucidated by analysis of the equation [7]:

$$E_{1/2} = \xi - \frac{0.059}{n} \log \frac{K_s f_a}{K_a f_s} \tag{2}$$

where K_s and K_a are constants of proportionality in the Ilkovich equation, $605\, nD^{1/2} m^{2/3} t^{1/6}$, that describes the diffusion process in the aqueous solution and in mercury; $\underline{f_s}$ and $\underline{f_a}$ are the corresponding activity coefficients; and ξ is a constant that depends upon the nature of the substance being reduced. As the ionic strength is increased, the activity of the ions of the metals being polarographed decreases, and the $E_{1/2}$ is shifted toward the negative. Harden, for example, found that when the concentration of hydrochloric acid was changed twentyfold, the increase in ionic strength produces a shift of the $E_{1/2}$ totaling 10-15 millivolts, which is practically within the limits of experimental error. The change in $E_{1/2}$ may go as high as 100.0-200.0 millivolts when the concentration of the principal electrolyte is varied over a wide range (from 0.01 to 10.0 N) [7].

The presence of dehydrating substances in the solution may also affect the half-wave potential of reducible nickel and cobalt appreciably. When the ions of the "indifferent" electrolyte react with the ions of the metals under study, as is most often manifested by the formation of complex ions, their half-wave potentials shift perceptibly toward the negative by diminishing the actual concentration of free ions [6,8,9]. The concentration of the "indifferent" electrolyte most affects the half-wave potentials of nickel and cobalt in the irreversible process of their reduction. The magnitude of the shift of the half-wave potentials of the nickel and cobalt complex ions is a measure of their stability and makes it possible to establish the structure of the compounds formed by calculating the coordination number (p) from the equation [7]:

$$p = \frac{\Delta E_{1/2}\, n}{0.059\, \Delta \log C_x} \tag{3}$$

where $\Delta E_{1/2}$ is the difference in the half-wave potentials measured at different concentrations of the complex-ion constituent (in volts); n is the number of electrons taking part in the reduction process; and $\Delta \log C_x$ is the difference between the logarithms of the concentration of the complex-ion constituent.

When reversible complex ions of nickel and cobalt are formed, there is no difference between the diffusion current of their electrolytic reduction and that of simple ions, inasmuch as there is practically no difference between the rate of movement of such complex ions and that of simple ions.

In irreversible reduction the amplitude of the diffusion wave is not always linearly proportional to the concentration of the ion being reduced. Soviet researchers, for example, have found that when nickel chloride is reduced in an "indifferent" solution of ammonium chloride containing gelatin, the relationship between the amplitude of the nickel polarographic wave and its concentration in solution is represented by a straight line that does not pass through the origin [10]. In the polarographic determination of nickel in an ammonium cyanide medium, we use an empirical calibration straight line that likewise does not pass through the origin [11]. We used the fundamental equation for a polarographic wave:

$$E_{de} = E_{1/2} - \frac{0.059}{n} \log \frac{i}{i_d - i} \tag{4}$$

where E_{de} is the applied emf (in volts), i is the current at the given point of the volt-ampere curve (in microamperes) and i_d is the limiting current (in microamperes) to test the reversibility of the process of nickel and cobalt reduction.

We have determined the nature of the electrode polarization of nickel and of cobalt in all the media specified above, using the slope of the straight line in the graph. From Equation (4) we get:

$$\tan \alpha = \frac{\Delta E_{de}}{\log \frac{i}{i_d - i}} = \frac{0.059}{n}. \tag{5}$$

The values of the slope found experimentally for the irreversible electrolytic reduction of nickel and cobalt agree with the values calculated theoretically. Whenever the slope found experimentally differs markedly from the theoretical figure, it is evidence of the presence of chemical as well as concentration polarization.

In this research we have investigated electrode polarization in comparatively dilute solutions of "indifferent" electrolytes, which affords several advantages over the use of concentrated solutions: sensitivity of the electrode reaction, choice of conditions for the joint deposition of the metals, and the like.

EXPERIMENTAL

The polarographic solutions we used were $1 \cdot 10^{-5}$ molar solutions of nickel and cobalt sulfate. The pH was measured by the usual electrochemical method, using a hydrogen electrode. We used a 1946 M-7-2000 visual polarograph and a mirror galvanometer with an absolute sensitivity of $1.2 \cdot 10^{-9}$ amp/mm. The distance from the galvanometer mirror to the scale was 0.25 m. Each measurement was repeated 2-8 times at the same galvanometer sensitivity. Two capillaries were used, their constants being given in Table 1.

TABLE 1

Capillary No.	Capillary constant $m^{2/3}t^{1/6}$, $mg^{2/3}\ sec^{-1/2}$	Mg. of mercury flowing out per sec, $\underline{m}$	Seconds required for the effluence of 1 drop of mercury, $\underline{t}$	Remarks
1	2.10	2.61	1.83	Employed in Tests 1-12 of Table 2, Tests 1-11 of Table 3, and in the tests of Fig. 5.
2	1.82	1.89	2.40	Employed in Tests 12-16 of Table 3 and the tests of Fig. 2.

In some instances small maxima appeared in the polarograms; they were suppressed by two drops of 0.5% gelatin or phenol red (per 10.0 ml of solution).

a) Investigation of Electrode Polarization in the Electrolysis of Nickel and Cobalt in Ammoniacal Solutions

We investigated the influence of the following substances upon the volt-ampere curves of nickel and cobalt: 1) ammonium hydroxide; and 2) ammonium chloride containing 1.25 moles of ammonium hydroxide per liter. Our results are given in Table 2.

TABLE 2

Effect of $\underline{C}_{NH_4OH}$ and $\underline{C}_{NH_4Cl}$ upon the Amplitude of the Polarographic Wave of Nickel and Cobalt and upon their $\underline{E}_{1/2}$

Test No.	Concentration		Nickel				Cobalt			
	NH_4OH (mole/liter)	NH_4Cl (mole/liter)	Wave height, mm.	Diffusion current, microamps	$E_{1/2}$, volts	Reduction potential $\underline{E}$, volts	Wave height, mm.	Diffusion current, microamps	$E_{1/2}$, volts	Reduction potential $\underline{E}$, volts
1	0.1	0.05/0.1	40.0	4.80	−1.00	−0.96	30.0	3.60	−1.430	−1.31
2	0.5	0.05/0.1	41.0	4.92	−1.08	−1.06	55.0	6.60	−1.320	−1.25
3	1.0	0.05/0.1	42.0	5.00	−1.13	−1.09	55.0	6.66	−1.370	−1.33
4	1.5	0.05/0.1	40.0	4.80	−1.16	−1.13	55.0	6.66	−1.380	−1.35
5	2.0	0.05/0.1	37.5	4.50	−1.18	−1.16	57.0	6.84	−1.401	−1.36
6	4.0	0.05/0.1	36.0	4.32	−1.22	−1.17	60.0	7.20	−1.451	−1.40
7	1.25	0.05	43.0	5.16	−1.15	−1.09	55.0	6.60	−1.370	−4.32
8	1.25	0.10	43.0	5.16	−1.15	−1.08	55.5	6.66	−1.370	−1.31
9	1.25	0.20	43.0	5.16	−1.16	−1.10	56.5	6.78	−1.380	−1.31
10	1.25	0.30	42.5	5.12	−1.17	−1.10	56.5	6.78	−1.380	−1.32
11	1.25	0.50	41.0	4.92	−1.19	−1.12	57.5	6.90	−1.390	−1.33
12	1.25	1.0	39.5	4.74	−1.20	−1.13	59.5	7.14	−1.40	−1.34

Note: In Column 3, the figure 0.05 refers to nickel, the 0.1 figure referring to cobalt.

According to the results of Tests 1-6 (Table 2), the nickel diffusion current increases but little at ammonium hydroxide concentrations ranging from 0.1 to 1.0 moles/liter, due to gradual dehydration and the formation of ions whose volume is less. The current reaches a maximum when the ammonium hydroxide concentration is 1 mole/liter, after which it slowly drops with increasing concentration of this complex ion constituent up to 4.0 moles/liter. This is apparently due to an increase in the absolute quantity of complex ammoniacal molecules of nickel, plus an increase in their stability in accordance with the law of chemical equilibrium. As the concentration of ammonium hydroxide is increased, the half-wave potential of nickel is shifted toward the negative, which is evidence of the formation of a complex ion in the solution.

An interesting phenomenon is observed when cobalt is electrolyzed in an ammoniacal medium. As the ammonia concentration is raised from 0.1 to 0.5 mole/liter, the diffusion current of this element rises sharply at first (from 3.60 to 6.60 microamps), though the current rises slowly thereafter as the concentration of this complex-ion constituent is further increased to 4.0 moles/liter, reaching a limiting value of 7.20 microamps. This phenomenon is apparently related to the disintegration of the stable aqueous complex ion of cobalt with the coordination number

6, producing considerable overvoltage during electroreduction, and the formation of an ammoniacal complex ion.

When the hexahydrate complex cobalt ion is converted into an ammoniacal ion, the number of free simple ions of cobalt rises abruptly, and the half-wave potential is sharply shifted toward the positive. Any further increase in the ammonia concentration merely causes a shift in the equilibrium of the ammoniacal complex ions and the simple ions, so that the rise in the negative reduction potential is smooth.

We plotted the curve of $\log \frac{i}{i_d - i}$ as a function of $\underline{E}_{de}$, shown in Figure 1, in order to study the nature and magnitude of the electrode polarization occurring in the electrolysis of nickel and cobalt in solutions of a complex-ion constituent. The nickel slope gradually increases as the ammonia concentration is raised (Fig. 1, c). Inasmuch as the retardation of electrolytic reduction at a dropping mercury electrode cannot be attributed to retarded electrocrystallization of the metal, as is the case with a platinum electrode, the difference between the experimentally determined slope and the theoretically calculated value of 0.029 volt may be considered to be the result of retarded decomposition of the complex ammoniacal ion of nickel [13]. The polarographic findings indicate that we can assign the formula of $[Ni(NH_3)_6]^{\cdot\cdot}$ to the complex ion, since we got a value approximating six when we computed the coordination number from Equation 3 (Table 4).

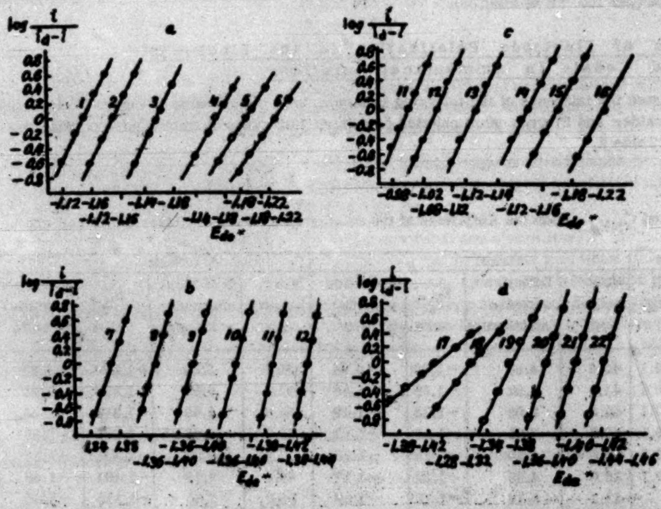

Fig. 1. Electrode polarization in the electrolysis of nickel and cobalt as a function of the concentration of NH_4OH and NH_4Cl. a) Rise in chemical polarization in the electrolysis of nickel as the concentration of NH_4Cl is raised, the NH_4OH concentration being 1.25 moles: 1) 0.05 molar NH_4Cl, $\tan \measuredangle = 0.049$; 2) 0.1 molar NH_4Cl, $\tan \measuredangle = 0.050$; 3) 0.2 molar NH_4Cl, $\tan \measuredangle = 0.050$; 4) 0.3 molar NH_4Cl, $\tan \measuredangle = 0.055$; 5) 0.5 molar NH_4Cl, $\tan \measuredangle = 0.065$; 6) 1.0 molar NH_4Cl, $\tan \measuredangle = 0.071$.

b) Rise in chemical polarization in the electrolysis of cobalt: 7) 0.05 molar NH_4Cl, $\tan \measuredangle = 0.035$; 8) 0.1 molar NH_4Cl, $\tan \measuredangle = 0.033$; 9) 0.2 molar NH_4Cl, $\tan \measuredangle = 0.032$; 10) 0.3 molar NH_4Cl, $\tan \measuredangle = 0.032$; 11) 0.5 molar NH_4Cl, $\tan \measuredangle = 0.030$; 12) 1.0 molar NH_4Cl, $\tan \measuredangle = 0.030$.

c) Increase in the nickel slope with increasing concentration of NH_4OH: 11) 0.1 NH_4OH, $\tan \measuredangle = 0.043$; 12) 0.5 molar NH_4OH, $\tan \measuredangle = 0.047$; 13) 1 molar NH_4OH, $\tan \measuredangle = 0.048$; 14) 1.5 molar NH_4OH, $\tan \measuredangle = 0.050$; 15) 2 molar NH_4OH, $\tan \measuredangle = 0.054$; 16) 4 molar NH_4OH, $\tan \measuredangle = 0.056$.

d) Increase in the nickel slope with increasing concentration of NH_4OH in the reduction of cobalt: 17) 0.1 molar NH_4OH, $\tan \measuredangle = 0.121$; 18) 0.5 molar NH_4OH, $\tan \measuredangle = 0.042$; 19) 1 molar NH_4OH, $\tan \measuredangle = 0.042$; 20) 1.5 molar NH_4OH, $\tan \measuredangle = 0.030$; 21) 2 molar NH_4OH, $\tan \measuredangle = 0.030$; 22) 4 molar NH_4OH, $\tan \measuredangle = 0.030$.

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* Standard calomel electrode.

TABLE 3

Effect of the Concentration of Ammonium Oxalate and of the Solution pH upon the Diffusion Current of Nickel and Cobalt and upon their $E_{1/2}$

Test No.	Concentration		Solution pH	Nickel				Cobalt			
	NH_4OH (mole/liter)	Ammonium oxalate (mole/liter)		Wave height, mm.	Diffusion current, microamps	$E_{1/2}$ volts	Reduction potential E, volts	Wave height, mm.	Diffusion current, microamps	$E_{1/2}$ volts	Reduction potential E, volts
1	–	0.05	5.1	35.0	1.68	−0.95	−0.75	43.0	2.06	−1.08	−0.87
2	–	0.05	6.0	36.0	1.72	−1.02	−0.80	45.0	2.16	−1.08	−0.89
3	–	0.05	7.0	37.0	1.78	−1.08	−0.85	47.0	2.26	−1.08	−0.89
4	–	0.05	8.0	40.0	1.92	−1.18	−0.88	49.0	2.35	−1.09	−0.90
5	–	0.05	10.0	70.0	3.36	−1.33	−1.20	112.0	5.38	−1.36	−1.25
6	–	0.01	10.0	19.0	2.28	−1.19	−1.11	–	–	–	–
7	–	0.05	10.0	28.5	3.42	−1.31	−1.22	49.0	5.88	−1.35	−1.25
8	–	0.10	10.0	38.0	4.56	−1.36	−1.29	60.0	7.20	−1.39	−1.29
9	–	0.15	10.0	40.0	4.80	−1.37	−1.33	56.0	6.72	−1.40	−1.32
10	–	0.20	10.0	39.0	4.68	−1.38	−1.34	50.0	6.00	−1.40	−1.33
11	–	0.30	10.0	37.0	4.56	−1.38	−1.34	45.5	5.46	−1.45	−1.40
12	0.05	0.10	–	20.0	2.40	−1.15	−1.08	31.5	3.78	−1.40	−1.33
13	0.10	0.10	–	25.0	3.00	−1.13	−1.06	32.5	3.90	−1.38	−1.32
14	0.50	0.10	–	26.0	3.12	−1.15	−1.09	33.0	3.96	−1.39	−1.34
15	1.00	0.10	–	26.5	3.18	−1.15	−1.08	34.0	4.08	−1.40	−1.35
16	1.50	0.10	–	27.0	3.28	−1.19	−1.10	34.5	4.14	−1.43	−1.38

Note: During polarography of solutions, the galvanometer sensitivity was S = 1/10 (in Tests 1-5); in all other tests S = 1/25.

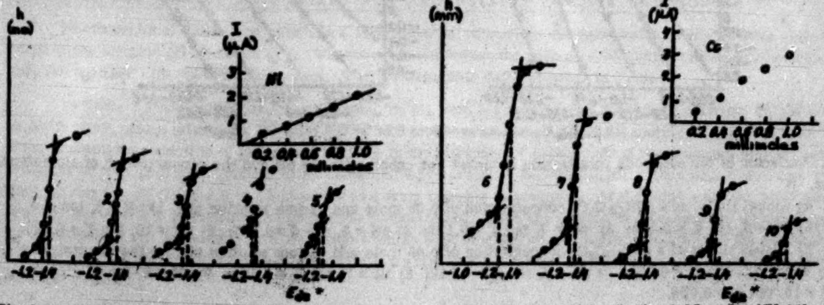

Fig. 2. Calibration lines for nickel and cobalt in their electrolysis in 0.1 molar NH_4Cl + 1.25 molar NH_4OH.
*Standard calomel electrode.

The curves showing the variation of $\frac{i}{i_d - i}$ with E_{de} in the polarography of cobalt (Fig. 1, d) are evidence of appreciable polarization at low ammonia concentrations; raising the concentration of the ammonia solution diminishes the chemical polarization at the cathode. There is no chemical polarization present in a 1.5-molar solution of ammonium hydroxide; hence, the hexahydrate complex ion of cobalt causes greater retardation of electrolytic reduction than does the ammonia complex ion. Other research workers [16] have also observed a decrease in chemical polarization in electrolysis during the reduction of ammoniacal complex ions, as compared to the hexahydrate cobalt ion.

The coordination number was found to approximate six (Table 4); hence, we can say that there are hexammine cobaltic ions in the solution. The slight discrepancy between the values of the coordination number found by polarography in ammonia and the theoretical figure of 6 may be attributed to the incomplete transformation of the complex hexahydrate ion into a hexammine ion with a coordination number of 6. Some ions of other composition

TABLE 4

Coordination Numbers of Complex Ions of Nickel and Cobalt in Ammonia and Oxalate Solutions

Complex-ion constituents	Ratio of concentrations of complex-ion constituents (C_2/C_1)	Nickel		Cobalt	
		Difference of half-wave potentials, $\Delta E_{1/2}$	Coordination number, p	Difference of half-wave potentials, $\Delta E_{1/2}$	Coordination number, p
Ammonia	0.5/0.1	0.080	3.90	—	—
	1.0/0.5	0.050	5.72	0.05	5.72
	2.0/1.5	0.021	5.70	0.021	5.70
	4.0/2.0	—	—	0.05	5.72
Ammonium oxalate at pH = 10	0.10/0.05	0.05	5.72	—	—
	0.15/0.10	0.017	3.25	0.01	1.98

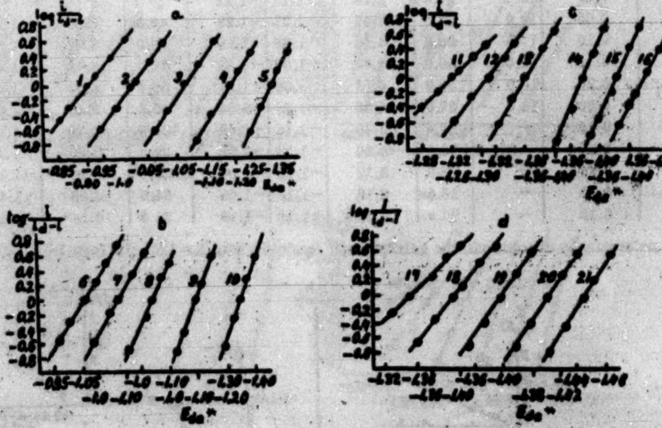

Fig. 3. Variation of the electrode polarization of nickel and cobalt with the pH and the concentration of ammonium oxalate.

a) Nickel slopes at a $(NH_4)_2C_2O_4$ concentration of 0.05 mole and various solution pH: 1) pH = 5, $\tan \measuredangle = 0.217$; 2) pH = 6, $\tan \measuredangle = 0.190$; 3) pH = 7, $\tan \measuredangle = 0.189$; 4) pH = 8, $\tan \measuredangle = 0.167$; 5) pH = 10, $\tan \measuredangle = 0.123$.

b) Nickel slopes at a $(NH_4)_2C_2O_4$ concentration of 0.05 mole and various solution pH, for the electrolysis of cobalt: 6) pH = 5, $\tan \measuredangle = 0.159$; 7) pH = 6, $\tan \measuredangle = 0.149$; 8) pH = 7, $\tan \measuredangle = 0.120$; 9) pH = 8, $\tan \measuredangle = 0.093$; 10) pH = 10, $\tan \measuredangle = 0.089$.

c) Effect of $(NH_4)_2C_2O_4$ concentration upon the electrode polarization of nickel at a pH = 10; 11) 0.01 molar $(NH_4)_2C_2O_4$, $\tan \measuredangle = 0.123$; 12) 0.05 molar $(NH_4)_2C_2O_4$, $\tan \measuredangle = 0.043$; 13) 0.1 molar $(NH_4)_2C_2O_4$, $\tan \measuredangle = 0.044$; 14) 0.15 molar $(NH_4)_2C_2O_4$, $\tan \measuredangle = 0.035$; 15) 0.2 molar $(NH_4)_2C_2O_4$, $\tan \measuredangle = 0.039$; 16) 0.3 molar $(NH_4)_2C_2O_4$, $\tan \measuredangle = 0.047$.

d) Effect of $(NH_4)_2C_2O_4$ concentration upon the electrode polarization of nickel a at a pH = 10, for the electrolysis of cobalt: 17) 0.05 molar $(NH_4)_2C_2O_4$, $\tan \measuredangle = 0.090$; 18) 0.1 molar $(NH_4)_2C_2O_4$, $\tan \measuredangle = 0.039$; 19) 0.15 molar $(NH_4)_2C_2O_4$, $\tan \measuredangle = 0.047$; 20) 0.2 molar $(NH_4)_2C_2O_4$, $\tan \measuredangle = 0.062$; 21) 0.3 molar $(NH_4)_2C_2O_4$, $\tan \measuredangle = 0.060$.

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*Standard calomel electrode.

may be formed, in which not all the 6 coordinated positions are filled by ammonia molecules, one or more of the positions being occupied by polar molecules of water, as in the complexes of the $[\mathrm{CO(NH_3)}_n\mathrm{(H_2O)}_m]^{\cdot\cdot}$, type, where the sum of n and m totals 6. Mendeleev [14], Grinberg [15], and others have commented on the possibility that such complex ions exist.

When the concentration of ammonium chloride is raised, while the ammonia concentration of 1.25 moles/liter is held constant, practically no change occurs in the diffusion current of nickel or cobalt; only at concentrations of ammonium chloride ranging from 0.3 to 1.0 mole/liter does the height of the nickel polarographic wave drop, the height of the cobalt wave rising slightly due to a change in the mobility of the complex molecules. Our findings on the decrease in the amplitude of the polarographic waves of nickel agree with the findings of Usatenko and Lyalikov, who state that ammonium chloride in the presence of ammonia almost does not suppress the wave of this metal at all [11].

Under these conditions the half-wave potentials of nickel and cobalt are gradually made more negative, which may be attributed to a shift of the equilibrium between the hexammine ions and the simple ions toward a decrease in the number of the latter, as well as to an increase in the ionic strength of the solution as the concentration of the ammonium chloride is increased. When we examine the curve of $\log \frac{i}{i_d - i}$ as a function of E_{de}, we see how chemical polarization gradually and slowly increases with an increase in the concentration of NH_4Cl during the electrolysis of nickel (Figure 1, a); at the same time, Figure 1, b shows that the slopes found from the cobalt polarograms are in good agreement with the theoretical value, 0.029, which is evidence of the reversibility of the electrode reaction involved in the reduction of cobalt.

As a result of our study of electrode polarization during the electrolysis of nickel and cobalt in a buffer solution of NH_4OH and NH_4Cl we have found the optimum conditions at which the diffusion current is a maximum, the polarographic wave is most distinct, and the reproducibility of the polarographic measurements is at its best. These were the conditions used in plotting the straight lines for these metals at concentrations ranging from $1 \cdot 10^{-3}$ to $1 \cdot 10^{-4}$ mole/liter (Figure 2). It has been found that diffusion current is a linear function of the concentration of the metals tested. This linearity is disturbed when the ammonium chloride solution contains no ammonia, the calibration straight line no longer passing through the origin.

b) Electrode Polarization in the Electrolysis of Nickel and Cobalt in Oxalate and Ammoniacal Oxalate Solutions

Polarography of nickel and cobalt in a 0.05 molar solution of ammonium oxalate could be done only at values of the solution pH in excess of 4. When the pH was lower, the polarographic waves of the metals under study ran together with the hydrogen waves. The polarographic data are given in Table 3.

As Table 3 indicates (Tests 1-6), changing the pH from 5.1 to 8.0 raises the diffusion current only slightly for both metals, while raising the pH from 8.0 to 10.0 produces an abrupt rise in the current of approximately 100% in the electrolytic reduction of nickel and of 150% in the reduction of cobalt. When the hydrogen ion concentration is lowered to a certain limit (pH 5.0 to 8.0), the half-wave potential becomes slightly more negative. After this limit, raising the pH (from 8.0 to 10.0) produces a sharp increase in potential. At the same time the polarogram slopes decrease with a diminishing hydrogen ion concentration, which is evidence of a decrease in chemical polarization (Figure 3,a). Apparently, the transition from an acid medium to an alkaline one involves the production of complex ions of different composition, causing a sharp rise in the diffusion current and a shift in the half-wave potential (Table 3).

We also made a study of the behavior of cobalt and nickel ions when the concentration of ammonium oxalate was varied (Table 3) while the pH was held constant at 10.0. Increasing the concentration of the ammonium oxalate solution from 0.01 to 0.10 mole/liter resulted in a sharp increase in the nickel and cobalt diffusion current and in an appreciable shift of their half-wave potentials toward the negative. Whereas a further increase in the ammonium oxalate concentration to 0.30 mole/liter produced practically no rise in the diffusion current during the reduction of nickel, the i_d dropped appreciably during the reduction of cobalt, exhibiting a maximum in a 0.1 molar solution of ammonium oxalate. The cobalt diffusion current vanished in a saturated solution of the oxalate. The half-wave potential, which remained practically constant in the case of nickel, decreased, even though only slightly, in the case of cobalt. The slopes of the nickel polarograms for various concentrations of ammonium oxalate are reproduced in Figure 3,c. These slopes indicate that, in conformity with the foregoing assertions concerning the changes in i_d and $E_{1/2}$, the chemical polarization diminishes as the concentration of the tested complex-ion constituent is raised to 0.10 mole/liter, this polarization practically disappearing in a 0.15 molar solution and rising again as the ammonium oxalate concentration is raised still higher. The decrease in chemical polarization as the ammonium oxalate concentration is raised is due to dehydration of the complex nickel hexahydrate ion, while the rise in the i_d is due to a decrease in the volume of the resulting complex nickel oxalate ion because of the rearrangement of the coordinated groups in the inner sphere of the complex ion. Calculation of the coordination number yielded values of 6 and 3 (Table 4). The transformation of the complex nickel ion with coordination number 6 into a complex ion with coordination number 3 (Table 4) is due to a change in the inner sphere of the complex ion. It may be regarded as established that the C_2O_4'' group usually occupies two coordination positions in the formation of stable coordination compounds, the compounds in which the oxalate ion occupies one coordination position being less stable and being readily converted into a more stable form. In this case, a complex nickel ion in which all six positions are occupied by C_2O_4'' groups is formed at comparatively low concentrations of ammonium oxalate. As the concentration of oxalate ions is increased, the stability of the complex ion grows, due to the formation of a compound in which each C_2O_4'' group occupies two coordination positions. Thus we get the value of 3 when we calculate the p for complex ions that are formed in solutions containing a high concentration of ammonium oxalate.

The slopes of the cobalt polarograms (Figure 3,d) are evidence of a decrease in cathodic polarization as the concentration of ammonium oxalate rises. This decrease in polarization during the electrolysis of cobalt does not, however, attain the level required for reversibility of the reaction. In the electrolytic reduction of nickel, however, the electrode reaction becomes reversible under these conditions.

Thus, these findings indicate that the complex cobalt hexahydrate ion is decomposed more slowly than the ammonia and oxalate ions (at a pH = 10.0).

When we computed the coordination number of cobalt we got values that were close to 2 (Table 4). Here again, we have a rearrangement within the inner sphere of the complex ion, resulting in a lowering of the coordination number to 2. The circumstance that the figure of 4.50 calculated from the experimental data differs substantially from the value of 4.0 is due, in our opinion, to the presence of a small percentage of complex ions with coordination number 6 in the solution.

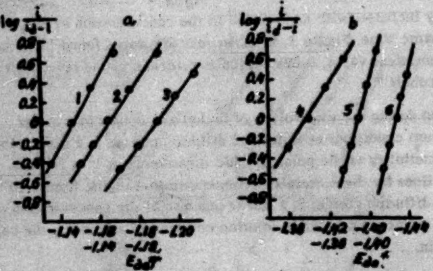

Fig. 4. Variation of the slope in the electrolysis of nickel and cobalt in an ammonia-oxalate solution whose $(NH_4)_2C_2O_4$ concentration = 0.1 mole/liter.

a) Electrolysis of nickel: 1) 0.05 molar NH_4OH, $\tan \sphericalangle = 0.066$; 2) 0.5 molar NH_4OH, $\tan \sphericalangle = 0.074$; 3) 1.5 molar NH_4OH, $\tan \sphericalangle = 0.080$.

b) Electrolysis of cobalt: 4) 0.05 molar NH_4OH, $\tan \sphericalangle = 0.062$; 5) 0.5 molar NH_4OH, $\tan \sphericalangle = 0.029$; 6) 1.5 molar NH_4OH, $\tan \sphericalangle = 0.029$.

*Standard calomel electrode.

We likewise investigated the variation of the nickel and cobalt vole-ampere curves with the ammonia concentration when 0.1 mole/liter of ammonium oxalate was present. The results of our experiments are given in Table 3 (Tests 12-16). As we see from these experimental figures, the nickel and cobalt $E_{1/2}$ does not change perceptibly as the ammonia concentration is increased; the diffusion current of both metals, however, rises, even though only slightly, due to the production of more highly mobile ions. As in the instances of the electrolysis of nickel in a $NH_4OH - NH_4Cl$ buffer solution considered previously, the polarization rises with an increase in the concentration of ammonium hydroxide, this polarization being most pronounced in an ammonia-oxalate solution (Figure 4,a). As for the polarization occurring in the electrolysis of cobalt in this same basic solution, the slopes indicate that chemical polarization is suppressed when the ammonia concentration is sufficiently high (Figure 4,b). Thus it is ammonia that exerts the principal influence upon the volt-ampere curve in an ammonia-oxalate medium. Calibration lines were plotted for both metals at concentrations ranging from $1 \cdot 10^{-3}$ to $1 \cdot 10^{-4}$ mole/liter, and at the optimum conditions of a pH of 10 and an approximately 0.125 molar solution of ammonium oxalate. We found that the nickel and cobalt i_d was a linear function of the ammonium oxalate concentration, the straight line passing through the origin (Figure 5).

SUMMARY

1. A study has been made of the nature of electrode polarization in the electrolysis of nickel and cobalt sulfates at a dropping mercury electrode with different complex-ion constituents present. It has been found that an

irreversible electrolytic reduction of nickel and cobalt takes place in some buffer mixtures of NH_4OH and NH_4Cl and ammonia-oxalate solutions.

2. It is suggested that the reason for the irreversible reduction of nickel and cobalt at a dropping mercury electrode from complex ions formed in the media specified above is the stable hydration that prevents the instantaneous decomposition of the complex ion. When the hydrate layer is broken down, even when more stable but less highly hydrated coordination compounds are formed, the chemical polarization is either diminished or disappears completely, which is evidence of the occurrence of a reversible electrolytic reduction of the nickel and cobalt ions.

3. It has been shown experimentally that when NH_4OH is present (within a certain concentration range), the complex nickel and cobalt oxalate ions break down, forming ammonia ions.

4. The variation of the amplitude of the nickel and cobalt diffusion waves with their concentration in the media we have tested has been checked, and it has been established that the equation: $\underline{i_d} = \underline{KC}$ holds under these conditions.

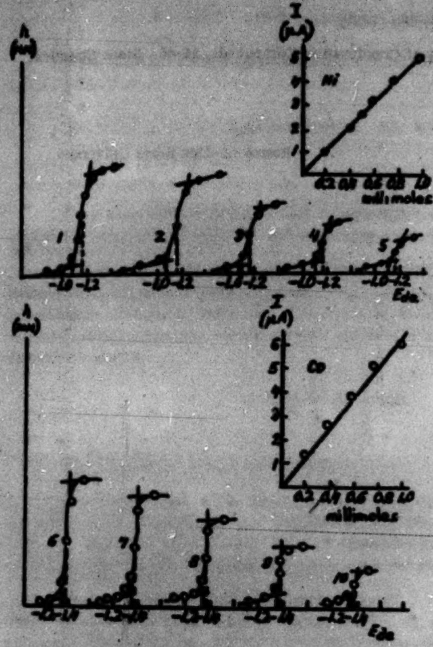

Fig. 5. Calibration lines of nickel and cobalt in their electrolysis in a 0.125 molar solution of $(NH_4)_2C_2O_4$ at a pH = 10.

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Received October 6, 1950

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STUDY AND CLASSIFICATION OF THE COMPOUNDS IN THE SULFUR TRIOXIDE–NITROGEN PENTOXIDE–WATER SYSTEM

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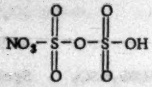
It has been definitely established by now that three individual compounds of definite chemical composition exist in the solid crystalline state, all containing sulfur trioxide in addition to nitrogen pentoxide.

The pioneer in the investigation of compounds of this type was Weber [1], who isolated two crystalline compounds as far back as 1864: $N_2O_5 \cdot 4SO_3 \cdot H_2O$ and $N_2O_5 \cdot 4SO_3 \cdot 3H_2O$. The first of these compounds, $N_2O_5 \cdot 4SO_3 \cdot H_2O$, or, writing it differently, $HNO_3 \cdot 2SO_3$, was again produced and described in 1949 by Amelin and Borodastova [2]. The two authors regard the compound they synthesized as a nitratopyrosulfonic acid and assign it the following structural formula:



$$NO_3-\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}-O-\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}-OH$$

The crystals had a m.p. of + 106.5°.

In the same year, 1949, Dode and Pascard [3] synthesized Weber's other compound: $N_2O_5 \cdot 4SO_3 \cdot 3H_2O$, which the authors assert "had never been synthesized since Weber's time in 1864", and "about which practically nothing is known, neither its physical and chemical properties nor its structure." Dode effected their synthesis under complicated experimental conditions, using low temperatures and pressures.

Dode and Pascard found the melting point of the compound they had produced was +32°, though they advanced no structural formula for it. Lastly, in 1907 Pictet and Karl [4] synthesized and described the anhydrous compound $N_2O_5 \cdot 4SO_3$, which they called nitrilotetrasulfate. This compound proved to be highly stable. Its melting point was +124° and its boiling point +220°. The authors assigned it the following structural formula:

$$O_2N-O-SO_2-O-SO_2-O-SO_2-O-SO_2-O-NO_2.$$

All the three specified compounds are apparently representatives of a single type:

$$N_2O_5 \cdot 4SO_3 \cdot \underline{m}H_2O, \tag{1}$$

where $\underline{m}$ is zero, one, and three.

Any further increase in $\underline{m}$, i.e., in the number of water molecules added, results in the formation of a system that is liquid at ordinary temperatures, in which Hantzsch [5], Usanovich [6], and other researchers, including ourselves [7], have succeeded in detecting a partially dissociated individual compound of the same type, in which $\underline{m}$ equals five, i.e., $N_2O_5 \cdot 4SO_3 \cdot 5H_2O$ or $N(OH)_3(HSO_4)_2$.

Moreover, we have succeeded in experimentally proving, by the iodometric method, that a compound of a totally different type:

$$N_2O_5 \cdot 2SO_3 \cdot nH_2O, \tag{2}$$

where $\underline{n} = 3$ to wit: $N_2O_5 \cdot 2SO_3 \cdot 3H_2O$, or according to Hantzsch, $[NO_3H_2]HSO_4$, is present in concentrated liquid sulfuric-nitric mixtures.

In the experimental section of this paper we report some further results of our investigations of the $N_2O_5-SO_3-H_2O$ ternary system through as wide a range as possible of its existence in the liquid state. We used the viscosimetric method of physicochemical analysis in these investigations.

EXPERIMENTAL

Using the viscosity method proved to be quite feasible, since even those compounds in the $N_2O_5-SO_3-H_2O$ system that are solid at room temperature, which fuse when the temperature is raised, exhibit an exceptional tendency toward supercooling, persisting in the liquid state even at temperatures that are dozens of degrees below the melting point.

As we know, another feature of the viscosity method is the fact that this method may be employed to confirm the presence of only a single compound in the system in question, even when other methods definitely establish the presence of several coordination compounds. Apparently, viscosimetry detects only that compound, of those formed within the system, which is partially dissociated into its constituent molecules to the least degree.

The results of our experimental measurements of the viscosity in the nitric acid—pyrosulfuric acid at the three temperatures of 0, 20, 30.2° are listed in Table 1 and illustrated in Figure 1.

As we see from the data, the viscosity maximum at 0 and 20° corresponds to a composition of:

$$HNO_3 \cdot H_2S_2O_7 \cdot \text{ or } N_2O_5 \cdot 4SO_3 \cdot 3H_2O$$

The viscosity maximum at 30.2° is shifted somewhat toward pyrosulfuric acid, i.e., the more viscous component, which must be related to the increasing dissociation of the compound. Hence, the existence of the compound $N_2O_5 \cdot 4SO_3 \cdot 3H_2O$ in the liquid as well as the solid state must be regarded as definitely established.

TABLE 1

Viscosity of the $HNO_3-H_2S_2O_7$ System

HNO_3		Viscosity, centipoises		
% by weight	Molar %	0°	20°	30.2°
0.0	0.0	—	57.2	37.5
7.4	18.5	—	91.2	56.9
15.0	33.3	—	97.8	72.6
19.8	41.1	543.4	138.8	81.8
23.1	46.0	—	154.2	**93.9**
26.2	50.1	**574.9**	**161.9**	86.7
30.4	55.2	—	117.7	68.9
31.9	57.1	—	103.5	62.6
35.9	61.3	231.3	72.8	45.9
40.1	65.4	156.8	53.4	34.2
45.1	69.9	95.7	34.5	23.5
50.2	74.0	58.2	23.1	16.1
60.1	81.0	25.1	11.3	8.3
70.0	86.8	11.8	5.9	4.9
80.0	91.9	5.6	3.1	2.4
90.0	96.2	2.6	1.6	1.3

TABLE 2

Viscosity of the HNO_3-SO_3 System at 30.2°

HNO_3		Viscosity, centipoises
% by wt.	Molar %	
14.6	17.8	234.7
21.7	26.0	1046.0
25.6	29.7	**1074.3**
27.6	32.6	971.6
33.5	39.0	921.4
45.0	51.0	410.4
69.9	74.7	12.4
80.9	84.4	3.5
95.1	93.6	1.2

TABLE 3

Specific Viscosity of the $HNO_3-H_2SO_4$ System at 20.8°

HNO_3		Specific gravity, $d_4^{20.8}$	Viscosity, centipoises
% by weight	Molar %		
0.0	0.0	1.8300	23.2
8.5	12.7	1.8744	29.2
13.1	19.0	1.8683	30.5
17.1	24.4	1.8641	30.6
20.3	28.4	1.8534	29.0
22.8	31.4	1.8475	27.8
30.9	41.0	1.8206	22.0
38.2	49.0	1.7955	16.8
45.2	56.3	1.7692	13.4
55.3	65.8	1.7305	8.5
67.5	76.4	1.6794	4.7
76.6	83.6	1.6401	2.9
88.5	92.3	1.5812	1.6
100.0	100.0	1.5113	0.9

Another representative of the same stable $N_2O_5 \cdot 4SO_3 \cdot mH_2O$ type may be detected in a no less distinct form when we investigate the internal friction in the HNO_3-SO_3 system (Table 2 and Figure 2). Due to the high temperature (30.2°), the viscosity maximum in this system is shifted somewhat toward the more viscous component SO_3, but the very high relative and absolute values of the maximum viscosity are evidence of the intensity of the chemical interaction between the components. We have not yet been able to measure the internal friction at a lower temperature.

Thus, the existence of a $HNO_3 \cdot 2SO_3$ or a $N_2O_5 \cdot 4SO_3 \cdot H_2O$ compound in the liquid state as well as in the solid state must also be regarded as fully established.

When we compare the maximum values of viscosity at the same temperature (30.2°) in the HNO_3-SO_3 system (Table 2), and the $HNO_3-H_2S_2O_7$ system (Table 1), we notice the rapid drop in the absolute

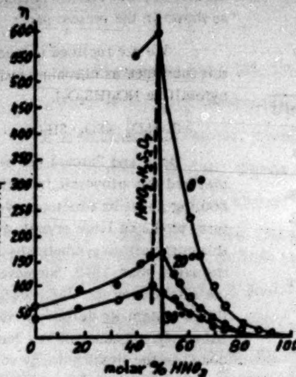


Fig. 1. Viscosity of the $HNO_3-H_2S_2O_7$ System.

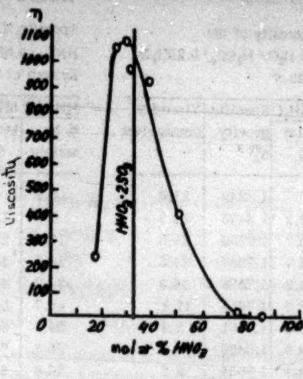


Fig. 2. Viscosity of the HNO_3-SO_3 System at 30.2°.

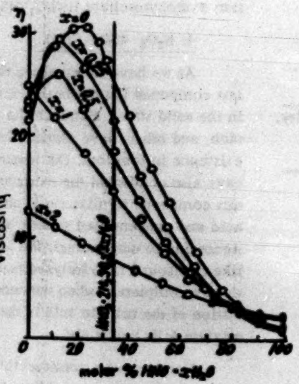


Fig. 3. Viscosity of the $HNO_3 \cdot xH_2O-H_2SO_4 \cdot xH_2O$ System at 20.8°.

viscosity as the percentage of water in the system increases (1074.3 and 93.9 centipoises). This is probably due to a decrease in the stability of the individual members of the $N_2O_5 \cdot 4SO_3 \cdot mH_2O$ series as the value of the coefficient m rises, i.e., as the number of molecules of water entering into the composition of the molecule of the complex compound is increased.

We ran a series of experiments in which we measured the viscosity of the $HNO_3 \cdot xH_2O-H_2SO_4 \cdot xH_2O$ system, where x = 0, 0.25, 0.5, 1.0 and 2.0, to shed more light on this question.

Our results are listed in Tables 3-7 and illustrated in Figure 3.

Classification of the compounds found. Present-day information on the properties of mixtures of nitric acid with sulfuric acid and oleums of various concentrations [8], based chiefly upon study of the products of electrolysis and analysis of Raman spectra, indicates that these mixtures contain nitrogen-containing cations and anions with the composition of HSO_4^- and $HS_2O_7^-$. Collating these data with the research results set forth in the present paper, we shall attempt to suggest a classification of the various members of the $N_2O_5 \cdot 4SO_3 \cdot mH_2O$ series whose existence has been most reliably established.

We now believe the individual members of this series to be the following individual saltlike compounds:

1. $N_2O_5 \cdot 4SO_3$.

Pictet and Karl called this highly stable compound nitrilotetrasulfate. We think that the structure of this substance, which is crystalline at room temperature, is like that of potassium tetrachromate, so that we shall call it nitronium tetrasulfate.

2. $N_2O_5 \cdot 4SO_3 \cdot H_2O$

Amelin and Borodastova have called this compound nitratopyrosulfonic acid monohydrate. We have also synthesized the beautifully formed crystals of this hydrate. What is more, we have established the presence of this compound beyond the shadow of a doubt in our study of the liquid system HNO_3-SO_3 not only by the volumetric

TABLE 4

Specific Viscosity of the $HNO_3 \cdot 0.25\ H_2O - H_2SO_4 \cdot 0.25H_2O$ System at 20.8°

$HNO_3 \cdot 0.25H_2O$		Specific	Viscosity,
% by weight	Molar %	gravity, $d_4^{20.8}$	centipoises
0.0	0	1.8342	21.6
8.4	12.2	1.8476	29.9
17.0	23.7	1.8230	26.8
25.9	34.7	1.7937	21.6
35.2	45.2	1.7596	16.0
44.9	55.3	1.7255	11.1
54.9	64.9	1.6861	7.3
65.2	74.0	1.6436	5.1
76.4	83.1	1.5954	2.7
87.9	91.7	1.5430	1.6
100.0	100.0	1.4907	1.1

TABLE 5

Specific Viscosity of the $HNO_3 \cdot 0.5H_2O - H_2SO_4 \cdot 0.5H_2O$ System at 20.8°

$HNO_3 \cdot 0.5H_2O$		Specific	Viscosity,
% by weight	Molar %	gravity, $d_4^{20.8}$	centipoises
0.0	0.0	1.8230	22.9
8.8	12.6	1.8112	26.1
16.9	23.2	1.7854	22.6
25.9	34.2	1.7552	18.1
35.2	44.7	1.7229	13.7
44.7	54.2	1.6863	9.5
54.8	64.4	1.6474	6.8
65.3	73.7	1.6068	4.3
76.0	82.5	1.5673	2.9
87.8	91.4	1.5228	1.9
100.0	100.0	1.4762	1.3

TABLE 6

Specific Viscosity of the $HNO_3 \cdot H_2O - H_2SO_4 \cdot H_2O$ System at 20.8°

$HNO_3 \cdot H_2O$		Specific	Viscosity,
% by weight	Molar %	gravity, $d_4^{20.8}$	centipoises
0.0	0.0	1.7721	24.9
8.4	11.6	1.7445	21.7
17.0	22.7	1.7159	18.3
26.0	33.5	1.6865	14.5
35.3	43.9	1.6546	11.7
45.0	53.9	1.6221	8.5
54.9	63.6	1.5874	6.4
65.3	72.9	1.5527	4.6
76.4	82.3	1.5168	3.4
88.1	91.4	1.4806	2.4
100.0	100.0	1.4445	1.7

TABLE 7

Specific Viscosity of the $HNO_3 \cdot 2H_2O - H_2SO_4 \cdot 2H_2O$ System at 20.8°

$HNO_3 \cdot 2H_2O$		Specific	Viscosity,
% by weight	Molar %	gravity, $d_4^{20.8}$	centipoises
0.0	0.0	1.6450	12.6
8.6	11.3	1.6196	11.0
17.5	22.3	1.5942	9.5
26.6	32.9	1.5686	8.0
35.6	43.2	1.5430	6.7
45.7	53.3	1.5173	5.7
55.7	63.0	1.4913	4.6
66.1	72.6	1.4653	3.8
76.9	81.8	1.4389	3.1
88.2	91.0	1.4128	2.5
100.0	100.0	1.3860	2.1

method [9], but also by viscosimetry, as shown in the present paper.

We are inclined to regard this substance as nitronium hydropyrosulfate $NO_2[HS_2O_7]$.

3. $N_2O_5 \cdot 4SO_3 \cdot 3H_2O$.

Dode and Pascard, who synthesized this trihydrate in 1949, say nothing about its structure. We, in turn, produced large crystals with this composition synthetically in the same year, 1949. Moreover, in our research on the $HNO_3 - H_2S_2O_7$ liquid system we definitely established the existence of this compound in the liquid state by volumetric analysis and by measuring the viscosity.

The chemical structure of the trihydrate may be that of nitracidium hydropyrosulfate $[H_2NO_3][HS_2O_7]$.

4. $N_2O_5 \cdot 4SO_3 \cdot 5H_2O$.

As we have stated above, this last compound has not been described in the solid state; Hantzsch, Usanovich, and others have assumed its existence in solutions. Our researches have also confirmed the existence of this compound in mixtures of nitric acid and concentrated sulfuric acid. According to our findings, this saltlike compound is hydrolyzed practically completely when the concentration of the sulfuric acid in the mixture falls below 92%.

Hantzsch also considers this hydrate to be hydronitracidium bisulfate $[H_3NO_3][HSO_4]_2$.

5. Our experimental researches indicate that other members of the $N_2O_5 \cdot 4SO_3 \cdot mH_2O$ series than those listed, with an m higher than five, do not exist even in the partially dissociated state.

SUMMARY

1. Several compounds of distinct chemical structure have been found to exist in the liquid ternary system nitrogen pentoxide—sulfur trioxide—water, constituting individual members of a series whose general formula is $N_2O_5 \cdot 4SO_3 \cdot mH_2O$.

2. Some of the members of this series have been isolated in the crystal state.

3. The stability of these compounds decreases as the coefficient m increases, i.e., as the amount of water entering into the compound rises. At values of m in excess of 5 compounds of this type do not exist in the liquid state, even in a partially dissociated state.

4. An endeavor is made to classify the known individual compounds of the $N_2O_5 \cdot 4SO_3 \cdot mH_2O$ series.

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Received October 11, 1950

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INVESTIGATION OF THE VOLATILITY OF ALKALI ELEMENTS AT HIGH TEMPERATURE

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The information on the volatility of alkali chlorides at high temperature is rather contradictory. Gmelin [1] states that lithium chloride vaporizes at white heat. Hoermann [2] thinks that this salt begins to vaporize at red heat. According to Jaeger [3], lithium chloride vaporizes perceptibly at 960°. This process is extremely rapid above 1080°, the sublimate exhibiting an alkaline reaction when it is wetted with water. The same author states that sodium chloride vaporizes rapidly at 1080°, and very rapidly at 1150°. The reference literature [4] asserts that this compound is perceptibly volatile even at its melting point (i.e., at about 800°). Bunsen [5] notes that potassium chloride is more volatile than sodium chloride. Thürmer [6] believes that potassium chloride vaporizes even in the 200-250° range, evaporation increasing as the temperature rises to dark-red and bright-red heat. According to Jaeger, potassium chloride vaporizes appreciably at 980°, vaporization being very rapid at 1160°. As this author says, the vapor of the salt has an acid reaction, that of the residue dissolved in water being alkaline.

Kirchhoff and Bunsen [7] noted the volatility of rubidium chloride when heated. Jaeger considers that perceptible vaporization of rubidium chloride begins at 950°.

According to Jaeger, cesium chloride begins to vaporize at 925°, the salt evaporating very rapidly at 1000°. Kastler [8] states that cesium chloride is stable in the 300-525° range, beginning to vaporize only at approximately 700°. Marked vaporization is observed at 800°. Kirchhoff and Bunsen assert that cesium chloride is the most volatile of all the chlorides of the alkali elements.

The experimental data in the literature on the vapor pressure of the alkali chlorides usually refer to temperatures above 800-900°. It is not impossible, of course, that the vapor pressure of these compounds is high enough even below these temperatures for perceptible evaporation of samples to occur.

The nature of the gaseous medium may affect the temperature at which vaporization of an alkali chloride sets in, in the opinion of several authors. Jander and Busch [9] found that the vaporization of rubidium chloride was perceptible at 470° in a current of gaseous hydrogen chloride, the corresponding temperature for cesium chloride being 450°. Zintl and Goubeau [10] found potassium chloride to be volatile at 600° in an atmosphere of hydrogen chloride.

The volatility of the alkali chlorides must be taken into account in analytical practice whenever the alkali element is recovered in one way or another from the object of analysis as a chloride and is then brought to constant weight by calcination. For the same reason it is important to regulate the temperature when alkali molybdates, wolframates, niobates, and similar compounds are analyzed by the hydrochlorination method, in which a sample of the substance is calcined in a current of hydrogen chloride, any alkali elements present being converted into chlorides and weighed as a nonvolatile residue.

We have made a thorough study of the temperature at which the perceptible vaporization of chlorides of all the alkali elements sets in in various gaseous media. The experiments were run in a tubular or crucible electric furnace. Temperatures were measured with a platinum-platinum-rhodium thermocouple calibrated at the melting points of zinc and silver. The 0.2-0.3 g samples of the chlorides were placed in porcelain boats, and a current of the given gas was passed through the operating tube at the specified velocity. Heating lasted 1 hour. We also measured the rate of vaporization of the alkali chlorides in air in open platinum crucibles. The temperature was raised in 50° steps in successive runs. The temperature at which vaporization sets in was taken to be that at which a loss of weight of at least 0.0002 g was detected. The initial preparations of the chlorides were analyzed for their chlorine content and found to be satisfactory (Table 1). Spectrum analysis indicated that the cesium chloride contained 0.07% potassium and 0.65% rubidium.

TABLE 1

Analysis of Chlorides of the Alkali Elements

Compound	% Chlorine	
	Found	Calculated
LiCl........	83.59	83.63
NaCl.......	61.22	61.41
KCl........	47.34	47.56
RbCl.......	29.38	29.32
CsCl.......	20.98	21.06

TABLE 2

Temperature at which Vaporization of Alkali Chlorides Sets In in Air (Calcination time 1 hour)

Temperature	Change in weight of the chlorides, g				
	LiCl (0.1857 g substance)	NaCl (0.2276 g substance)	KCl (0.2419 g substance)	RbCl (0.2464 g substance)	CsCl (0.2580 g substance)
400°	none	–	–	–	–
450	none	–	–	–	–
500	none	–	–	–	none
550	0.0007	–	–	none	0.0003
600	0.0005	–	none	none	0.0009
650	–	none	0.0003	0.0010	–
700	–	none	0.0012	0.0029	–
750	–	0.0014	–	–	–
Onset of perceptible vaporization	550°	750°	650°	650°	550°

Table 2 gives the results of our determination of the temperature at which the volatilization of the alkali chlorides sets in when they are calcined in air. The tests run in a current of air indicated that perceptible vaporization was observed in the same temperature range, though the loss in an air current exhibited a somewhat greater loss of weight than in calcination in air.

The lowest temperature at which vaporization sets in is exhibited by lithium and cesium chlorides (550°). Lithium chloride exhibits the highest temperature of perceptible vaporization (750°). Volatility increases as we pass from sodium chloride to the chlorides of potassium, rubidium, and cesium. The temperatures we have found for the onset of perceptible vaporization of the alkali chlorides differ considerably from the figures given in the literature, being lower than the earlier figures as a rule. It should be noted that all the alkali chlorides begin to vaporize much (approximately 50-100°) below their melting points (cf. Table 5).

TABLE 3

Temperature at which Alkali Chlorides Begin to Vaporize in a Current of Hydrogen Chloride (10 liters/hour). (Calcination time 1 hour).

Temperature	Change in weight of the chlorides, g				
	LiCl (0.2472 g substance)	NaCl (0.2505 g substance)	KCl (0.2324 g substance)	RbCl (0.2425 g substance)	CsCl (0.2514 g substance)
400°	none	–	–	–	–
450	none	–	–	–	–
500	none	–	–	–	none
550	0.0002	–	–	–	0.0013
600	–	–	–	none	0.0016
650	–	–	none	none	–
700	–	none	0.0002	0.0015	–
750	–	0.0012	0.0015	–	–
Onset of perceptible Vaporization	550°	750°	700°	700°	550°

We used the apparatus described by one of the present authors [11] in our study of the volatility of the chlorides in a current of hydrogen chloride. The porcelain boats usually absorb some HCl, and they were therefore first brought to constant weight by calcining them in a current of hydrogen chloride. The test results, given in Table 3, show that the alkali chlorides begin to vaporize perceptibly in an atmosphere of hydrogen chloride at practically the same temperature as in air.

The slight increase in the observed temperature at which vaporization sets in for the potassium and rubidium chlorides is less than 50°, the difference between the temperatures of successive runs. Thus, we are unable to confirm the Jander and Busch findings that the vaporization temperature of rubidium and cesium chlorides drops appreciably in an atmosphere of hydrogen chloride.

TABLE 4

Temperature at which Vaporization of Alkali Chlorides Sets In in a Current of Steam (6 g/hour)

Temperature	Change in weight of the chlorides, g				
	LiCl (0.2776 g substance)	NaCl (0.2256 g substance)	KCl (0.2076 g substance)	RbCl (0.2195 g substance)	CsCl (0.2112 g substance)
400°	none	–	–	–	–
450	none	–	–	–	none
500	0.0001	–	–	–	0.0001
550	0.0025	–	–	none	0.0008
600	0.0035	–	none	0.0006	0.0023[*]
650	–	none	0.0004	–	–
700	–	none	0.0019	–	–
750	–	0.0013	–	–	–
Onset of perceptible vaporization	550°	750°	650°	600°	550°

[*] The sample weighed 0.2124 g in this run initially.

Our temperature for the onset of vaporization of lithium chloride in a current of HCl agrees with our previous results as found in analyzing lithium wolframates [12].

Alkali chlorides were calcined in a current of steam as follows. A certain quantity of water was heated in a small conical flask, which was sealed with a stopper through which an outlet tube was passed. The steam passed into an operating quartz tube placed within an electric furnace and containing a boat with a sample of the chloride. The inlet section of the quartz tube was heated externally to 150-200° by means of a Bunsen burner to prevent condensation of the steam. The operating tube was connected to a glass collector flask fitted with a reflux condenser. Part of the chloride that vaporized at the respective temperature conditions settled on the colder wall of the quartz tube, the rest entering the collector together with the condensate. In view of the hygroscopicity of lithium chloride, the sample of this substance was heated to 400° for 30 minutes in a current of anhydrous air after the steam run.

TABLE 5

Comparison of the Melting Points and the Onset of Perceptible Vaporization of Alkali Chlorides in Various Gaseous Media

Alkali Chloride	M.p.	Onset of perceptible vaporization,(°)			Difference between the melting points and the temperatures at which vaporization of the alkali chlorides begins in air (round figures) (°)
		In air	In a current of HCl	In a current of steam	
LiCl....	605°	550°	550°	550°	50°
NaCl...	800	750	750	750	50
KCl....	770	650	700	650	120
RbCl...	726	650	700	600	75
CsCl...	646	550	550	550	100

Research has established that the vaporization of most of the alkali chlorides in a current of steam begins in the same temperature range as in the analogous calcination tests in the air. Only in the case of rubidium chloride is the temperature at which vaporization sets in lowered by 50° (Table 4).

It should be again emphasized that for most of the alkali chlorides (LiCl, NaCl, and CsCl) the temperatures at which vaporization begins is the same in the media tested. In an atmosphere of HCl potassium chloride begins to vaporize at a temperature that is 50° higher than in air or in a current of steam. In a current of HCl rubidium chloride vaporizes at a temperature that is 50° higher than in air, the respective temperature in steam being 50° lower than in air. Inasmuch as the experiments were run using temperature intervals of 50°, we may conclude that the nature of the gaseous medium has no substantial effect upon the temperature at which the alkali chlorides begin to vaporize. As Table 5 also indicates, the vaporization of the alkali chlorides begins to be perceptible at temperatures that are 50 to 120° below the melting points of the compounds in question. Lithium and sodium chlorides vaporize at temperatures closer to their melting points. The difference between the onset of vaporization and the melting point is much greater (some 75 to 120°) in the cases of potassium, rubidium, and cesium chlorides. The lowest temperatures at which vaporization sets in (550°) are found for lithium and cesium chlorides, these temperatures being nearly identical. The highest temperature at which vaporization begins is found in sodium chloride

(750°). The volatility of potassium and rubidium chlorides lies between that of sodium and cesium chlorides.

It may be postulated that the most volatile alkali chlorides are those in which the chemical bond is least typically ionic. Owing to the substantial polarizing action of the lithium ion, lithium chloride is one such chloride. Sodium chloride is more ionic, because of the increase in the cation's radius and its lesser polarizing effect, and, as we know, it has the highest melting point of all the alkali chlorides as well as the highest temperature for the onset of vaporization. The gradual increase in volatility as we pass to the chlorides of potassium, rubidium, and cesium may be caused by the deforming action of the chlorine ion upon the ion of the alkaline element, this action increasing with the increase in the radius of the latter. The appearance of a perceptible vapor pressure of the alkali chlorides at temperatures in the vicinity of their melting points forces us to conclude that the bond becomes less ionic and more polar when these substances are melted.

The results of the tests we have described afford some conclusions regarding the relative velocity of vaporization of the alkali chlorides in various gaseous media at temperatures in the vicinity of the point at which perceptible vaporization of these compounds begins. The loss of weight in a current of steam is, as a rule, several times greater than the loss of weight observed during calcining in air or in a current of hydrogen chloride (Table 6). An exception to this is sodium chloride, which exhibits an approximately equal loss of weight in all three of the media studied.

TABLE 6

Rate of Vaporization of Chlorides of the Alkali Elements at Temperatures in the Vicinity of the Onset of Perceptible Vaporization (Calcination time 1 hour. Samples weighing about 0.25 g).

Chloride	Temp. of run	% loss of weight		
		In air	In a current of HCl (10 l/hr)	In a current of steam (6 g/hr)
LiCl.....	550°	0.48	0.08	0.90
NaCl....	750	0.62	0.48	0.58
KCl.....	700	0.49	0.09	0.92
RbCl....	600	none	none	0.27
CsCl....	600	0.35	0.64	1.08

TABLE 7

Analysis of the Products of the Sublimation of Lithium and Cesium Chlorides in a Current of Steam (Heating for 30 min to 800°. Steam flow rate: 18 g/hr).

Chloride	% Chlorine in initial chloride	% Chlorine in the sublimation products		
		Calcination residue	Sublimate	Dry residue of condensate
LiCl....	83.59	82.96	83.12	81.47 ±2%
CsCl...	20.98	20.97	21.00	21.72 ±2%

Vikt. I. Spitsyn and V.I.Shostak [13] recently found that the rate of vaporization of normal alkali sulfates at high temperatures is likewise increased considerably in the presence of steam. This phenomenon is, therefore, apparently observable in many compounds.

Nothing conclusive can be said regarding the effect of hydrogen chloride. According to the data in Table 6, lithium, sodium, potassium, and rubidium chlorides exhibit a more or less significant decrease in volatility in hydrogen chloride, as compared to calcination in air, this decrease being least perceptible in sodium chloride. In the case of cesium chloride the loss of weight in a current of hydrogen chloride is greater than in air, but less than in a current of steam.

The problem of how the nature of the gaseous medium affects the rate of vaporization of various substances requires further study. In so far as steam is concerned, however, it may be assumed that its singular behavior is due to the same causes that are responsible for the action of liquid water upon substances dissolved in it. The rate at which the alkali chlorides vaporize increases with rising temperature and with an increase in the steam flow rate.

Analysis of the calcination residue, the sublimate in the tube, and the condensate in the receiver indicated that these products exhibited a neutral reaction in solution in the case of all the alkali chlorides. The sublimate and the calcination residue were analyzed for chlorine in the case of the lithium and cesium chlorides (Table 7). The samples of these salts (weighing about 0.1 g) were heated for 30 minutes to 800°. The sublimate weighed 0.040 to 0.045 g. The condensate contained 0.002-0.003 g of the vaporized chloride, as indicated by evaporating the condensate to dryness. The products were analyzed by the Mohr method. It was found that there was no appreciable difference between the composition of the sublimate and that of the initial substance or of the calcination residue. The analysis of the chloride in the condensate was done as a check. In view of the small percentages of the substance analyzed, the possible errors in the determination of the chlorine amounted to ± 2% in this case. Thus, the rapid vaporization of alkali chlorides in a current of steam at the comparatively low temperatures investigated involves no perceptible hydrolysis.

Cabot's findings on the hydrolysis of sodium chloride by superheated steam [14] evidently refer to a higher temperature. Sen, Sen-Gupta, and Das-Gupta [15] have observed only slight decomposition of sodium chloride by steam at 500-810°. Guthrie and Nance [16] have observed slight hydrolysis of lithium chloride in the 430-530° range. Briner and Roth [17], on the other hand, have found that alkali chlorides are appreciably decomposed by steam, forming hydrochloric acid, at 550° (decomposition of 0.5 to 1.2% in one hour). The extent of hydrolysis increased to 14-33% at 900°, depending upon the nature of the compound tested. The cited paper does not say how the vaporization of the alkali chlorides, which becomes quite noticeable at temperatures in excess of 550-750°, was taken into account. There is no doubt that a high percentage of the chlorine was eliminated from the sample by the direct vaporization of the chloride.

Our experimental findings indicate that steam causes no appreciable decomposition of alkali chlorides at temperatures in the vicinity of the latter's melting points. In this instance, vaporization is evidently more rapid than hydrolysis. These phenomena are of geochemical interest. The action of superheated steam upon deep rocks whose temperature is sufficiently high ought to promote the vaporization of alkali chlorides from these rocks and the migration of these compounds closer to the earth's surface.

SUMMARY

1. A study has been made of the temperature conditions under which perceptible vaporization of the alkali chlorides occurs in various gaseous media (air, hydrogen chloride, and steam).

2. In air vaporization has been observed to set in at the following temperatures:

LiCl	NaCl	KCl	RbCl	CsCl
550°	750°	650°	650°	550°

3. In a current of hydrogen chloride or of steam vaporization of these compounds has been found to set in at the same temperatures (±50°).

4. The alkali chlorides exhibit perceptible volatility at temperatures that are 50-120° below their respective melting points.

5. It has been found that alkali chlorides vaporize at a much higher rate in a current of steam than in air or in hydrogen chloride. This process is not accompanied by hydrolysis phenomena at the test temeratures employed (550-800°).

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Received October 12, 1950

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THE MECHANISM OF THE CATALYTIC TRANSFORMATIONS OF HYDROCARBONS OVER A VANADIUM CATALYST

VII. THE COMPARATIVE BEHAVIOR OF BINARY MIXTURES OF HEPTANE, HEPTENE AND TOLUENE

A. F. Plate and G. A. Tarasova

In our earlier researches on the behavior of individual heptane, heptene-1, and heptene-3 in the presence of a vanadium catalyst [1] we have shown that the aromatization reaction is accompanied by a reversible dehydrogenation – hydrogenation of heptane ⇄ heptene and we suggested that heptene is not the inevitable intermediate product of the aromatization of heptane. A study of the effect of the principal reaction products of the aromatization of heptane – heptene and toluene upon the aromatization of the heptane constituted an extension of our investigation of the role of heptene in the aromatization of heptane. With this in view, we aromatized binary mixtures consisting of heptane, heptene-1, and toluene. They are not many papers in the literature upon the aromatization of hydrocarbon mixtures of definite composition.

The aromatization of heptane-heptene mixtures containing 10% to 80% of heptene was investigated by Green [2]. According to that author, the percentage of toluene in the catalyzate decreases as the percentage of heptene in the mixture is raised. These findings are contradicted, however, by numerous observations that heptene is aromatized more readily than heptane. The conclusions reached by Green apparently depend upon the specific conditions under which his experiments were run: the use of a cracking catalyst (2% MoO_3 on Al_2O_3) and operation at high temperature (550°). Taylor and Fehrer [3] aromatized a mixture of heptane and 15% of heptene with a chrome catalyst and found that somewhat more toluene was produced from such a mixture than from pure heptane under the same conditions. We find the fullest data on the aromatization of hydrocarbon mixtures in R. D. Obolentsev and Yu. N. Usov [4], who explored the behavior of a series of alkane-alkene mixtures at 485° over a chrome contact catalyst. In particular, they investigated the aromatization of two mixtures containing heptane and 30 and 50%, respectively, of heptene-1, as well as the aromatization of each of these individual hydrocarbons. The authors showed that there is a direct relationship between the percentage of heptene in the mixture and the amount of toluene produced and concluded that "the mixture components undergo conversion independently of each other, as it were." Nor has much work been done upon the effect of adding toluene upon the aromatization of heptane. Oblad, Marschner, and Heard [5] aromatized a heptane mixture containing 25% of toluene at 482° with chromic oxide on alumina. The authors concluded that heptane mixed with toluene is aromatized in proportion to the concentration of heptane in the mixture. Green [2] aromatized several mixtures, containing 24 to 92% of toluene in addition to heptane. Although aromatization was accompanied by thermal cracking, the author concluded that the heptane is converted into toluene even when the initial mixture contains an appreciable percentage of toluene. We know of no papers in the literature on the aromatization of heptene in the presence of toluene.

The present paper is a report on the behavior of mixtures of heptane – heptene, heptane – toluene, and heptene – toluene under identical conditions of temperature, rate of flow, and length of run in the presence of the same sample of vanadium catalyst. Experiments with heptane – heptene mixtures have shown that the percentage of toluene in the catalyzate rises with an increase in the percentage of heptene in the mixture. This relationship is represented by a straight line like the one previously found by Obolentsev and Usov for a series of alkane-alkene mixtures in the presence of a chromic catalyst. We can therefore say that in a mixture of heptane and heptene each hydrocarbon is aromatized in proportion to its concentration. This conclusion is borne out by an experiment involving the aromatization of a mixture of heptane and 2-methylbutene-2 under the same conditions. We thought it would be interesting to aromatize heptane in the presence of an alkene that could not form a six-membered ring. It was found that the yield of toluene from such a mixture was the same as its yield from heptane alone, or, in other words, heptane reacts in this mixture in proportion to its concentration. Aromatization of heptane-toluene mixtures indicated that the amount of newly formed toluene was directly proportional to the percentage of heptane in the mixtures, whereas when heptene-toluene mixtures were aromatized, the amount of toluene formed was not a linear function of the percentage of heptene in the original mixture, the share of the reacting heptene rising sharply as its percentage in the mixture was decreased. Hence, heptane behaves differently in a mixture with toluene than heptene does, although each of them is aromatized in proportion to its concentration when mixed together. These contradictory conclusions cannot be reconciled if we assume that heptane and heptene are aromatized at the same active centers. But if we assume that these hydrocarbons are aromatized at different centers, the facts we ascertained are not mutually contradictory. Such an assumption appears to be highly probable in view of the complicated nature of the surface of a mixed oxide catalyst.

EXPERIMENTAL

The catalyst consisted of vanadium oxide deposited on alumina [1]. The catalyst was regenerated by air and then reduced with hydrogen before each series of tests. It exhibited no change of activity during this procedure.

Apparatus and operational procedure. The tests were made in the circulating system described by us previously. In this research we chose another method of liquid supply. Instead of an automatic buret we used a graduated cylinder with a piston [6], which was lowered evenly by the action of a motor, thus ensuring uniformity of the liquid supply. The temperature was 480° in all the tests. The volumetric rate was 0.5 in every run. The operational procedure was as follows. Each series of tests was run during a single day without turning off the furnace. A mixture of a certain composition was passed through for 30 minutes, after which hydrogen was blown through the catalyst (for 35 - 40 minutes). to drive off the catalyzate. Then a mixture of a different composition was run through, and so on. The pure components of the mixture was run through in the same series of tests, as a check on the activity of the catalyst. The percentage of unsaturated hydrocarbons was determined, as usual, by the bromine number method [8]. We employed the methods of specific and relative dispersions to determine the percentage of toluene [7]. The method of relative dispersions was first tested with artificial heptane-toluene and heptene-toluene mixtures.

Aromatization of heptane-heptene mixtures. In this series of tests we investigated the behavior of five mixtures containing 5 to 30% of heptene-1, as well as the behavior of pure heptene and heptane. The results of these tests are listed in Table 1 and shown graphically in Fig. 1. In this fiture Curve I represents the percentage of toluene in the catalyzate; it is a straight line, as we see. Curve II indicates the behavior of the heptene in this mixture, based on the change in the bromine numbers of the catalyzate. When the mixture contains less than 10% of heptene, the percentage of unsaturated compounds in the catalyzate increases (cf Table 1, Col. 10 and the left-hand branch of Curve II, Fig. 1). When the mixture contains more than 10% of heptene, its percentage in the catalyzate drops (cf Table 1, Col. 10, and the right-hand branch of Curve II, Fig. 1).

TABLE 1

Test No.	Original mixture					Catalyzate				
	Composition, mol. %		n_D^{20}	Bromine number	Per cent unsaturated	n_D^{20}	Bromine number	Per cent unsaturated		Per cent aromatics
	Heptane	Heptene						By weight of the catalyzate	± Δ %	
31^1	100	0	1.3875	0.0	0.0	1.3923	11.9	7.5	+ 7.5	6.0
31^2	95	5	1.3880	7.5	4.7	1.3942	13.9	8.7	+ 3.7	8.0
31^3	90	10	1.3887	15.9	10.0	1.3964	15.6	9.7	− 0.3	9.0
31^4	50	50	1.3933	79.3	49.1	1.4089	36.8	23.0	−26.0	24.0
31^5	25	75	1.3964	121.0	74.5	1.4190	57.9	35.6	−88.9	30.5
31^6	10	90	1.3983	144.9	88.9	1.4261	72.2	44.3	−44.6	37.0
31^7	0	100	1.3997	(163.3)1)	100.	1.4297	86.7	53.1	−46.9	40.5

Aromatization of a mixture of heptane and 2-methylbutene-2. We investigated the behavior of a single mixture, containing 22.7 mol.% of 2-methylbutene-2. The mixture was run through at 480° for five hours. The catalyzate was identified and then fractionated into a column with an efficiency of 40 theoretical plates. The analysis of the catalyzate and of its fractions is given in Table 2.

As the table indicates, the catalyzate was separated into four fractions, which represented the following

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1) Calculated.

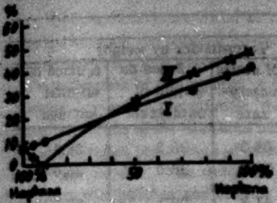

Fig. 1. Aromatization of heptane-heptene mixtures.

I - Per cent toluene in the catalyzates; II - change in the percentage of heptane in the catalyzates.

constituents: I—isopentene; II—heptene-heptane; III—heptane; and IV—heptane-toluene. When we compute the percentage of toluene in that portion of the catalyzate corresponding to the last three fractions, we get a figure of 8.9%. Comparing these results with Tests 31^1 (Table 1) and 34^6 (Table 3), in which the catalyzates produced by aromatizing heptane at the same temperature contained 6.0 and 8.5% of toluene, respectively, we may conclude that when mixed with 2-methylbutene-2, heptane is aromatized in proportion to its concentration. The heptene yield, based on Fractions II, III, and IV, was 7.1%, which also agrees with the results of Tests 31^1 and 34^6, in which the percentages of unsaturated compounds in the catalyzates totaled 7.5 and 7.2% respectively. When the heptenes were aromatized, we noted that they were partially hydrogenated [1]. In this instance of the aromatization of a mixture of heptane and 2-methylbutene, we again observed that the alkene was hydrogenated. The isopentene fraction contained 15% of saturated hydrocarbons.

The aromatization of heptane-toluene mixtures was explored in five mixtures, containing from 10 to 90% of toluene. The composition of the original mixtures and the test results are given in Table 3 and shown graphically in Fig. 2. Curve I indicates the percentage of newly formed toluene, while Curve II

TABLE 2

Fractionation and Analysis of the Fractions of the Catalyzate Produced from a Mixture of Heptane and 2-Methylbutene-2

Fraction	Boiling point at 760 mm, °C	Weight, grams	Weight, %	n_D^{20}	d_4^{20}	Bromine number	% Unsaturated		% Aromatics	
							Of the fraction	Of the catalyzate	Of the fraction	Of the catalyzate
Entire catalyzate		29.5	100	1.3912	0.6875	31.4	–	18.8	–	6.7
I	27.4-38.0	3.2	10.8	–	–	193.9	85.1	9.2	–	–
II	38.0-97.5	2.8	9.5	–	–	57.5	35.3	3.4	–	–
III	97.5-98.5	20.0	67.7	1.3912	0.6890	6.5	4.1	2.8	8.7	5.9
IV[1)]	98.5-101.0	3.3	11.1	1.4015	0.7070	3.0	1.8	0.2	20.0	2.2
	Residue	0.2	0.9	–	–	–	–	–	–	–
	Losses	None	–	–	–	–	–	–	–	–

TABLE 3

Aromatization of Heptane-Toluene Mixtures

Test No.	Original mixture			Catalyzate						
	Per cent by weight		n_D^{20}	n_D^{20}	Bromine number	% unsaturated, by weight		% aromatics, by weight		
	Heptane	Toluene				Of catalyzate	Of initial heptane	Of catalyzate	Δ, Based on weight of catalyzate	Δ, Based on initial heptane
34^6	100	0	1.3875	1.3956	11.7	7.2	7.2	8.5	8.5	8.5
34^2	90.0	10.0	1.3960	1.3960	14.6	9.0	10.0	16.0	6.0	6.7
34^1	77.0	23.0	1.4075	1.4139	11.2	6.8	8.8	30.0	7.0	9.1
34^3	49.5	49.5	1.4325	1.4363	8.9	5.3	10.7	53.0	3.5	7.1
34^5	26.5	73.5	1.4606	1.4646	3.3	1.9	7.2	76.3	2.8	10.6
34^4	10.0	90.0	1.4805	1.4803	1.8	1.0	10.0	89.0	(1)	(10)

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1) Distilled from a Würtz flask.

TABLE 4

Aromatization of Heptene - Toluene Mixtures

Test No.	Original mixture			Catalyzate						
	% by weight					% unsaturated by weight		% aromatics by weight		
	Toluene	Heptene	n_D^{20}	n_D^{20}	Bromine number	of entire catalyzate	$\pm\Delta$	of entire catalyzate	Δ, Based on weight of catalyzate	Δ, Based on original heptane
32^8	0	100	1.3997	1.4245	112.0	67.2	− 32.8	38.3	38.3	38.3
33^7	0	100	1.3997	1.4277	105.0	62.8	− 37.2	36.0	36,0	36.0
32^6	11.2	88.8	1.4078	1.4332	94.1	55.5	− 33.3	41.3	30.1	33.9
33^3				1.4370	87.4	52.0	− 36.8	46.0	34.8	39.2
32^7	21.5	78.5	1.4163	1.4400	85.6	50.8	− 27.7	48.0	26.5	33.8
33^6				1.4456	72.5	42.9	− 35.6	54.7	33.2	42.3
32^5	30.8	69.2	1.4232	1.4494	68.6	40.9	− 28.3	58.7	27.9	40.3
32^3	50.9	49.1	1.4411	1.4649	43.8	25.6	− 23.5	72.7	21.8	44.4
33^1				1.4638	43.7	25.6	− 23.5	72.0	21.1	43.0
33^2				1.4625	46.6	27.3	− 21.8	71.5	20.6	42.0
33^4	76.2	23.8	1.4674	1.4813	19.5	11.3	− 12.5	88.0	11.8	49.6
32^1	90.2	9.8	1.4838	1.4919	5.6	3.1	− 6.7	96.5	6.3	64.3
32^2				1.4925	4.6	2.6	− 7.2	97.5	7.3	74.5
33^4	94.7	5.3	1.4897	1.4924	6.5	3.8	− 1.5	97.2	2.5	47.2
33^5	100	0	1.4965	1.4951	1.6	0.9	+ 0.9	99.4	–	–

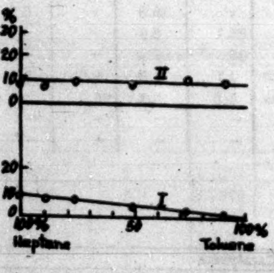

Fig. 2. Aromatization of heptane - toluene mixtures.

I - Percentage of toluene formed; II - toluene yield, based on initial percentage of heptane.

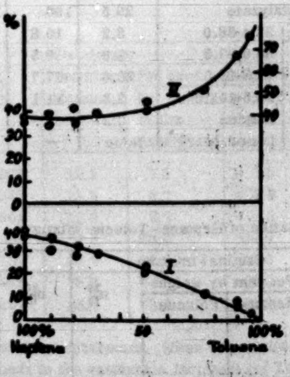

Fig. 3. Aromatization of heptene - toluene mixtures.

I - Per cent of toluene produced; II - toluene yield, based on the percentage of the original heptene.

gives the toluene yield, based on the initial percentage of heptane. The results of these tests indicated that the percentage of newly formed toluene is directly proportional to the percentage of heptane in the mixture, while the percentage of toluene, based on the heptane in the mixture remains constant.

Aromatization of heptene-toluene mixtures. Seven mixtures, containing from 11 to 95% toluene, were tested. We ran two sets of tests, the results being fairly well reproducible. Moreover, in both sets we aromatized pure heptane, while in one set we passed toluene over the catalyst.

The test results are listed in Table 4 and shown graphically in Fig. 3. Curve 1 represents the percentages of reacted heptene and toluene produced, the respective points coinciding, thus constituting a single curve. As the graph indicates, this function is expressed by a slightly convex curve. Curve II in Fig. 3 represents the toluene yield as a function of the heptene concentration in the mixture. To judge from this curve, the smaller the percentage of heptene in the mixture, the larger the proportion of the heptene that reacts. Inasmuch as the graphs showing the results of all the three binary mixtures have been plotted in the following coordinates: mixture composition versus percentage of toluene produced, the shapes of these curves indicate how these hydrocarbons displace one another. The straight line in Fig. 2, which represents the aromatization of heptane - toluene mixtures, shows that heptane and toluene are adsorbed at the surface of the catalyst in proportion to their concentrations. Heptane and heptene are adsorbed in the same manner (Fig. 1), while heptene is better adsorbed than toluene (upper curve in Fig. 3). This discrepancy between the behavior of heptane and heptene may be due to the fact that heptane and heptene are aromatized at different active centers in an oxide catalyst. In this case, it would seem that heptene is not necessarily an intermediate product in the aromatization of heptane.

SUMMARY

1. A study has been made of the aromatization of heptane-heptene mixtures at 480° over a catalyst consisting of vanadium oxide deposited upon alumina; it has been found that the percentage of toluene formed is directly proportional to the percentage of heptene in the mixture.

2. It has been shown that when the percentage of heptene in the mixture is below 5%, its percentage in the catalyzate increases, when its percentage is 10%, the percentage in the catalyzate remains constant, and when its percentage exceeds 10%, the percentage of unsaturated compounds in the catalyzate falls below the initial percentage.

2. A mixture of heptane and 2-methylbutene-2 (22.7 mol.%) has been aromatized at 480°. It has been found that the heptane in the mixture yields toluene and heptene in proportion to its concentration. Under these conditions part of the isopentene is hydrogenated to isopentane.

3. A study has been made of the effect of adding toluene (ranging from 10 to 90%) upon the aromatization of heptane at 480°. It has been found that the percentage of newly produced toluene is directly proportional to the percentage of heptane in the mixture; correspondingly, the toluene yield remains constant, based upon the percentage of the initial heptane.

4. A study has been made of the effect of adding toluene (ranging from 11.8% to 95.0%) upon the aromatization of heptene at 480°. It has been shown that the toluene yield, based upon the initial heptene, rises as the concentration of heptene in the mixture falls.

5. Comparison of the results of aromatization of the three binary mixtures: heptane-heptene, heptane-toluene, and heptene-toluene, seems to indicate that heptane and heptene are aromatized at different active centers of the catalyst.

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Received, November 25, 1950

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SYNTHESIS OF HYDROCARBONS BY THE ACTION OF HEXACHLOROETHANE UPON ORGANOMAGNESIUM COMPOUNDS

V. V. Korshak and T. D. Kozarenko

In his research into the reaction of hexachloroethane with organomagnesium compounds with the objective of synthesizing hexaaryl and hexaalkyl ethanes, one of the present authors [1] discovered that the following reaction:

$$2RMgX + C_2Cl_6 \rightarrow R\cdot R + C_2Cl_4 + 2MgClX.$$

took place, instead of the expected ethanes being synthesized.

This principal reaction was paralleled by reduction of the hexachloroethane, so that we secured, in addition to tetrachloroethylene, lower chlorine derivatives of ethane: pentachloroethane, 1,1,1,2-tetrachloroethane, 1,1,2,2-tetrachloroethane, and trichloroethane.

Organomagnesium compounds prepared from bromobenzene, p-bromotoluene, α-bromonaphthalene, and ethyl bromide were used in our investigation of this reaction. The first three compounds yielded diphenyl, ditolyl, and dinaphthyl, respectively. Ethylmagnesium bromide yielded ethane and ethylene.

Inasmuch as this reaction might be of interest as a new method of synthesizing hydrocarbons, we have returned to it in the present paper, setting as our objective the determination of the conditions that might ensure adequately high yields of the hydrocarbons.

To do this, we investigated the reaction of hexachloroethane with the organomagnesium compounds prepared from bromobenzene, α-bromonaphthalene, benzyl chloride, ethyl bromide, and methyl iodide. We ran a series of tests with each of these substances, in which we varied the reaction temperature, the concentration of the reagents, and the process time. In addition, we investigated the influence of the nature of the solvent, testing diethyl ether, dibutyl ether, diisoamyl ether, and mixtures of the latter two with diethyl ether as media.

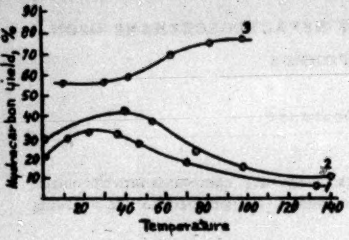
Our investigations indicated that this method made it possible to secure 33% to 79% of the theoretical yields of hydrocarbons, based on the halogen derivative employed in the reaction.

It is advisable to produce the organomagnesium compound in diethyl ether and then to add the hexachloroethane, dissolved in dibutyl or diethyl ether. Then part of the diethyl ether is driven off to fix the boiling point of the mixture at the optimum value. The optimum reaction temperature, producing the highest yield of the hydrocarbon, is 97° for benzyl chloride, 40° for bromonaphthalene, and 22° for bromobenzene. The yields drop off sharply above and below these temperatures, as may be seen from the figure.

When methylmagnesium iodide is reacted with hexachloroethane, it yields ethane and methane (39% and 61% respectively). Ethylmagnesium bromide yields a gas that consists chiefly of ethylene (77.8%) and contains 14.3% of ethane and 7.9% of butane.

It is worthy of note that the composition of this gas is close to the composition of the gas produced by Carothers [2] in the thermal decomposition of ethylsodium and of a coordination compound of the latter with diethylzinc (84.3% ethylene, 14.9% ethane, and 0.3% butane).

This may be regarded as confirming the idea we advanced earlier [1] to the effect that this reaction involves a stage in which free radicals are formed, so that the result depends upon the properties of the free radical. With aromatic radicals dimers are produced, whereas in the case of the unstable ethyl radical, which tends to split off hydrogen, there is only very little dimerization, the principal reactions being disproportionation ($2C_2H_5 = C_2H_4 + C_2H_6$) and the splitting off of hydrogen ($C_2H_5 = C_2H_4 + H$).



Hydrocarbon yield as a function of temperature.
1 - Diphenyl; 2 - dinaphthyl; 3 - dibenzyl.

Another factor serving to confirm the presence of free radicals in this transformation is the fact that a solution of an organomagnesium compound to which hexachloroethane has been added proves to be able to initiate the polymerization of styrene more vigorously than a solution of magnesium-ethyl bromide containing no hexachloroethane. As we know, the initiated polymerization of styrene and other polymerizable monomers sets in under the action of free radicals, produced by the decomposition of benzoyl peroxide or similar substances that can break down to yield free radicals [3]. It is therefore apparent that the solution of an organomagnesium compound gives off free radicals in the presence of hexachloroethane, that initiate the polymerization of styrene.

EXPERIMENTAL

Preparation of dibenzyl. Five grams of magnesium shavings and 70 ml of absolute ether were placed in a 500-ml four-necked flask fitted with a stirrer, a reflux condenser, a dropping funnel, and a thermometer. Then 30 g of benzyl chloride was added a drop at a time to the flask contents, with constant stirring (see Footnote 1). When nearly all the magnesium had dissolved, 25 g of hexachloroethane, dissolved in 70 ml of anhydrous n-dibutyl ether was added to the resultant organomagnesium compound (see Footnote 2). Part of the diethyl ether was driven off (via a straight condenser) to raise the boiling point of the reaction mixture to 80-90°. The mixture was kept at this temperature for 4 hours, after which the resultant coordination compound was decomposed with water and dilute sulfuric acid. The ether layer was dried over calcined calcium chloride and then fractionated in vacuo. The yield of dibenzyl with an m.p. of 51.2° was 16.6 g or 87% of the theoretical.

Other hydrocarbons may be produced in the same manner.

Footnotes. 1. When bromobenzene and α-bromonaphthalene are used, a crystal of iodine is added to the ether to shorten the induction period. 2. Whenever the temperature must not exceed +45°, it is advisable to substitute diethyl ether for the dibutyl ether.

SUMMARY

1. The reaction of hexachloroethane with organomagnesium compounds has been explored.

2. It has been shown that this reaction results in the formation of hydrocarbons that are dimers of the radicals making up the organomagnesium compound in the case of aromatic radicals and the methyl radical.

3. It has been shown that in the case of ethylmagnesium bromide only little butane is formed, the principal product being ethylene with some ethane.

4. It has been shown that organomagnesium compounds are initiators of the polymerization of styrene, especially when hexachloroethane is present.

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Received October 2, 1950.

THE ADDITION OF α-HALOGEN ETHERS OF THE $CH_3CHCl{-}O{-}R$ TYPE TO BUTADIENE

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Study of the order and mechanism in which halogens, halogen acids, hypohalogenous acids and their esters, and various halogenous organic compounds are added to butadiene is of considerable interest in organic chemistry. Not so long ago it was generally assumed, on the basis of the work of Thiele and other chemists, that the halogens and halogen acids are added to butadiene chiefly, or exclusively, at the 1,4 position, Thiele's notions, based on the assumption of the existence of partial valencies in carbon atoms, being used to explain the addition mechanism. Subsequently, with the development of electronic concepts in organic chemistry, a series of electronic schemas were proposed to explain the mechanism of addition; the most widespread acceptance being accorded to Ingold's and Burton's ionic mechanism (1928) [1]. More thoroughgoing investigation of the reactions involved in the addition of various reagents to butadiene, carried out in the past two decades, however, have shown that the findings of the earlier researches on the order in which addition occurred contained substantial errors in most instances, while in some cases they were wholly wrong. This is due to the fact that these researches either wholly ignored or else paid too little attention to the allyl rearrangements of the addition products (which are typical allylic isomers) that occur during the reaction, separation, and refining. More careful experiments, in which various precautions were taken to exclude or to reduce to a minimum the thermal isomerization of the addition products during the reaction and during the processing of the reaction mixture, have indicated that the halogens chlorine and bromine [2], and the halogen acids [3], are added to butadiene principally at the 1,2 position.

The papers by A.A. Petrov [4] and by B. A. Arbuzov and V.M. Zoroastrova [5] have shown that hypohalogenous acids and their esters are likewise chiefly added, and in some instances exclusively added, at the 1,2 position.

The problem of the order of addition of α-halogen ethers to butadiene had received hardly any attention in the literature prior to our recent papers. We used the addition of several α-halogen ethers of the general type of $CH_2Cl{-}O{-}R$ to show that it is the catalytic isomerization, rather than the thermal isomerization, of the chloroallylic isomers during the reaction processes occurring in the presence of zinc chloride or halides of other metals that is highly important in determining the order of addition of the alpha halogen ethers. This new and important factor was unknown prior to that time and hence could not be allowed for in earlier researches.

Allowing for catalytic isomerization, we found that 73-75% of chloromethyl ether [6] is added to butadiene at the 1,2 position, 25-27% being added at the 1,4 position, while 65-75% of chloromethyl ethyl and chloromethyl butyl ethers are added to butadiene at the 1,2 position, with 25-35% being added at the 1,4 position. This proved that the alpha halogen ethers, like the halogens, the halogen acids and the esters of hypohalogenous acids, are added to butadiene at the 1,2 position much more than at the 1,4 position.

In view of the theoretical interest of our results, we resolved to make a study of the addition of halogen ethers of the $CH_3CHCl{-}O{-}R$ general type to butadiene in the present research by way of an extension and expansion of our inaugurated researches. We prepared the halogen ethers in the usual manner, by reacting hydrogen chloride with a mixture of acetaldehyde and the corresponding alcohol, the addition to butadiene being effected by the procedure described in our preceding papers. 1)

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1) After our research had been completed there appeared a paper by Emerson, Deebel, and Longley [8], in which the authors describe the addition of several alpha halogen ethers to butadiene, referring to the paper by Straus and Thiele and to one of our papers. Many of the reactions carried out by the American authors have been described somewhat earlier in one of our reports [7]. They also secured the addition products of some alpha chloroethyl alkyl ethers to butadiene.

The addition of alpha chloroethyl methyl ether to butadiene in the presence of zinc chloride resulted in the following 1,2 and 1,4 addition products: 2-methoxy-6-chlorohexene-4 and 2-methoxy -4-chlorohexene-5. The overall yield of the addition products totaled 25%, the balance consisting of high-boiling products and tar. The alpha chloroethyl ethyl and alpha chloroethyl butyl ethers were added more smoothly, the overall yield of addition products totaling 50-60%. The addition of alpha chloroethyl ether to butadiene yielded approximately equal proportions of 2-methoxy-6-chlorohexene-4 and 2-methoxy-4-chlorohexene-5. Analogous results were obtained with alpha chloroethyl butyl ether, the products being 2-butoxy-6-chlorohexene-4 and 2-butoxy-4-chlorohexene-5.

The structure of the addition products was proved by their reactions with an alcoholic alkali and by the data of their catalytic isomerization, using the isomeric methoxychlorohexenes as examples. The reactions of an alcoholic alkali with halogenous allylic isomers provide a quite simple and convenient method of determining their structure, as we have shown in our previous papers [9]. When a primary halogen allyl isomer dissolved in methanol or ethyl alcohol is reacted with a potash alkali, only a single product is formed (the yield being high): an ether, the structure of which corresponds to that of the chloride used for the reaction, while when a secondary halogen allyl isomer is used under similar conditions, the products are a diene hydrocarbon and an ether of a secondary alcohol, mixed with a slight quantity of an ether of a primary alcohol in some instances.

$$R-CH_2-CH{=}CH-CH_2Cl + R'OH + KOH \rightarrow$$
$$\rightarrow R-CH_2-CH{=}CH-CH_2-OR' + KCl + H_2O$$
$$R-CH_2-CHCl-CH{=}CH_2 + R'OH + KOH \rightarrow R-CH{=}CH-CH{=}CH_2 +$$
$$+ R-CH_2-CH(OR')-CH{=}CH_2 + R-CH_2-CH{=}CH-CH_2OR'.$$

When a concentrated solution of an alkali in ethyl alcohol was reacted with the high-boiling isomer, we got nothing but an ether: 2-methoxy-6-ethoxyhexene-4, the yield being 63%. The low-boiling addition compound yielded 39% of a diene: 2-methoxyhexadiene-3,5 plus a mixture of ethers. The presence of a conjugated system of double bonds in the 2-methoxyhexadiene-3,5 was proved by its reaction with maleic anhydride, the reaction being quite vigorous. These results indicate that the high-boiling product is a primary halogen allyl isomer, while the low-boiling product is a secondary one.

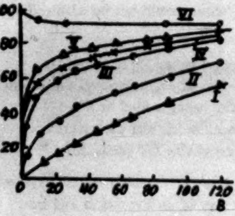


Fig. 1
A - Per cent 2-methoxy-6-chlorohexene-4 in the mixture; B - Time, days.

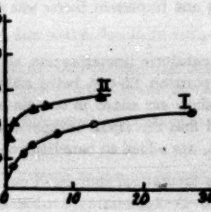
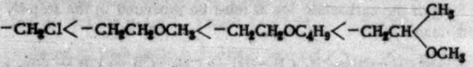


Fig. 2
A - Per cent 2-methoxy-6-chlorohexene-4 in the mixture; B- Time, days.

The structure of the addition products is also borne out by the findings of our study of their catalytic isomerization. Research into this problem is also of considerable theoretical interest on its own account, since it enables us to reach definite conclusions regarding the composition of an equilibrium mixture of halogen allyl isomers, besides providing data on the sequence and mechanism of the addition reactions. The catalytic isomerization of the methoxychlorohexenes was effected at temperatures of +20° and 0° in the presence of varying amounts of zinc chloride. The degree of isomerization of the chlorides was computed from the refractive indexes of the reaction mixtures as measured after given intervals of time. The results of our isomerization of the methoxychlorohexenes at +20° are shown in Fig. 1, the results for 0° being given in Fig. 2.

Curves I, II, III, IV, and V in Fig. 1 represent the isomerization of 2-methoxy-4-chlorohexene-5 containing 0.0022, 0.0044, 0.0066, 0.0077, and 0.012 mole of zinc chloride per mole of the chloride, respectively. Curve VI represents the isomerization of 2-methoxy-6-chlorohexene-4 when the molar concentration of zinc chloride is 0.012. In Fig. 2, Curves I and II represent the isomerization of 2-methoxy-4-chlorohexene-5 containing 0.0055 and 0.013 mole of zinc chloride per mole of the chloride. As we see from these graphs and from the tables given in the experimental section below, the rate of isomerization is increased as the temperature and the concentration of the catalyst in the reaction mixture are raised. The equilibrium state contains 90-93% of 2-methoxy-6-chlorohexene-4 and 7-10% of 2-methoxy-4-chlorohexene-5.

When we compare the compositions of equilibrium mixtures of isomeric methoxychlorohexenes, butoxychloropentenes [7], methoxychloropentenes, and dichlorobutenes [10], we find that their percentage of a primary halogen allyl isomer gradually diminishes, while that of the secondary isomer increases. This phenomenon is evidently due to a change in the structure of the substituent groups in these halogen allyl isomers, a gradual decrease in their induction effect. Thus, the radicals of the halogen allyl systems investigated by us in the present and preceding papers may be arranged in the following sequence:



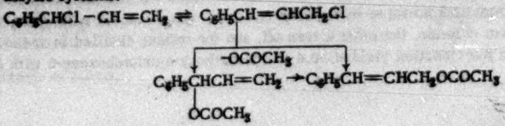
$$-CH_2Cl<-CH_2CH_2OCH_3<-CH_2CH_2OC_4H_9<-CH_2CH\genfrac{}{}{0pt}{}{CH_3}{OCH_3}$$

representing the order of their activity in shifting the equilibrium toward the formation of primary forms of the halogen allyl isomers or, what amounts to the same thing, the increasing value of their induction effect. We used the procedure described in our previous papers to determine the order in which alpha chloroethyl methyl ether was added to butadiene. In allowing for the catalytic isomerization of the isomeric methoxychlorohexenes during the reaction, we found that 65-75% of alpha chloroethyl methyl ether is added to butadiene at the 1,2 position and 25-35% at the 1,4 position at various temperatures and zinc chloride concentrations. These are figures of the same order of magnitude as in the addition of other alpha halogen ethers to butadiene [6,7].

Our results cannot be satisfactorily explained by means of the Ingold and Burton theory, as has been pointed out in our previous papers. In that theory it is assumed that addition is solely ionic and that, therefore, the ratio of the halogen allyl isomers produced as the result of addition must be of the same order of magnitude as their ratio in the state of equilibrium achieved in their thermal or catalytic isomerization, which likewise involve an ionic mechanism [6]. No such correspondence is found, however. As we have stated above, addition results in the formation of a mixture in which secondary (1,2 addition) halogen allyl isomers predominate, whereas isomerization results in predominantly primary halogen allyl isomers.

The discrepancy between Ingold's and Burton's ionic theory and the results of the last two decades of study of the addition of halogens, halogen and hypohalogenous acids, alpha halogen ethers, and other compounds to butadiene has evidently compelled the authors of this theory to return to a discussion of the mechanism of these reactions twenty years after the publication of that theory.

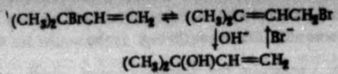
In a paper published in 1948, Mare, Hughes, and Ingold [11] assume that, besides the thermodynamic factor – the stability of the resulting butadiene addition products, the kinetic factor – the rate at which the isomers are formed – is also of considerable importance. On the basis of the conclusions concerning the kinetic factor derived from an examination of allyl rearrangements [12], these researchers assert that the decisive role governing the order of addition in the addition of halogen derivatives to butadiene and its homologs, which they believe to take place only ionically, is played by the kinetic factor, causing the addition to result in an isomer that is more advantageous kinetically though less stable thermodynamically. Although this amendment to the original theory brings it into agreement with the factual material available at the present time, the conclusions on the importance of the kinetic factor in the addition process, based upon analogies with the reactions of allylic systems:



$$C_6H_5CHCl-CH=CH_2 \rightleftharpoons C_6H_5CH=CHCH_2Cl$$

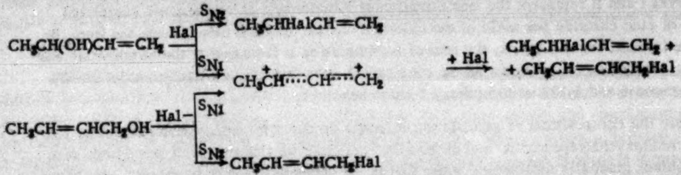
$$\downarrow\ -OCOCH_3\ \downarrow$$

$$C_6H_5\underset{OCOCH_3}{CH}CH=CH_2 \rightarrow C_6H_5CH=CHCH_2OCOCH_3$$

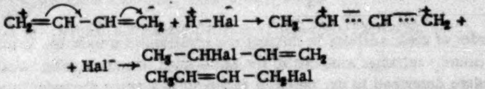


$$(CH_3)_2CBrCH{=}CH_2 \rightleftharpoons (CH_3)_2C{=}CHCH_2Br \quad \downarrow OH^- \ \uparrow Br^- \quad (CH_3)_2C(OH)CH{=}CH_2$$

cannot be regarded as sufficiently convincing in our opinion. The results of reactions involving the addition of halogen derivatives to butadiene must be compared with reactions of the following type:



in which there is a direct analogy with addition reactions of butadiene, rather than with the examples cited above, in which a kinetic factor is actually manifest but which exhibit no such direct analogy with butadiene addition reactions. In the halohydrination of butenyl alcohols, the reaction is largely monomolecular [13], yielding the same intermediate form of the carbonium ion as must be produced in the step-by-step addition of, say, hydrogen chloride to butadiene:



$$\overset{+}{C}H_2{=}CH{-}CH{=}\overset{-}{C}H_2 + \overset{+}{H}{-}\overset{-}{Hal} \rightarrow CH_3{-}\overset{+}{C}H \cdots CH \cdots \overset{+}{C}H_2 + {} + Hal^- \rightarrow \begin{matrix} CH_3{-}CHHal{-}CH{=}CH_2 \\ CH_3CH{=}CH{-}CH_2Hal \end{matrix}$$

The results of these two reactions are wholly different, however. In the case of addition, it is the secondary chloride that is chiefly produced (75% 1,2 addition), while it is a primary halide that is formed in monomolecular substitution. No appreciable kinetic factor is observed in the latter reactions, the ratio of the isomeric halides being close to that in the equilibrium mixture, readily attained in their thermal or catalytic isomerization. In several of our preceding papers, we have expressed the opinion, which we continue to maintain in the present paper, that the addition of various halogen derivatives to butadiene is not of the purely ionic type, but ionnomolecular in nature, in which polarization of the bonds during the process of addition does not attain complete dissociation in part of the added halogenated molecules. Depending upon the reaction conditions, the nature of the solvent, and that of the reagents, the ratio of the addition products formed ionically and molecularly may vary within wide limits. An important role in the addition process may apparently also be played by steric factors, whose importance was first pointed out by A.A. Petrov [4]. In the addition of halogen derivatives to homologs of butadiene and its derivatives with various substituent groups that are much more highly polarized than butadiene itself, addition occurs, apparently, only ionically, step-by-step; the addition reactions and the corresponding substitution reactions, in which we may suppose that the same intermediate carbonium ions are formed, result in the same ratios of isomeric halides, approaching their ratios in the equilibrium mixtures attained in the processes of thermal and catalytic isomerization.

EXPERIMENTAL

(with T. Galanina)

Addition of alpha chloroethyl methyl ether to butadiene. The following ingredients: 104 g of 1,3-butadiene (95%), 182 g of alpha chloroethyl methyl ether, and 2.9 g of freshly fused, pulverized zinc chloride, were successively added to a glass bottle immersed in a freezing mixture. The reaction mixture was allowed to stand in the freezing mixture for 10-15 hours. The ice melted during the first 5-6 hours, the reaction mixture remaining at room temperature for the remaining 5-10 hours. After this time had elapsed, the bottle containing the reaction mixture was again immersed in a freezing mixture, agitated vigorously a few times, and allowed to stand for 1-2 days. The end of the reaction was indicated by a drop of pressure inside the bottle. When the reaction was over, the reaction mixture was treated with several portions of water, its color changing from dark brown to light yellow. Then it was extracted with ether, the ether extract being dried over calcium chloride, the ether driven off, and the residue distilled in vacuo through a Widmer dephlegmator. Repeated fractionation yielded 30.4 g of 2-methoxy-4-chlorohexene-5 with a b.p. of 50° at 13 mm.

n_D^{20} 1.4349; d_4^{20} 0.9554; MR_D 40.54; calculated 40.45.
0.1934 g substance: 0.1832 g AgCl. Found %: Cl 23.5. $C_7H_{13}OCl$. Calculated %: Cl 23.9.

We also secured 41.8 g of 2-methoxy-6-chlorohexene-4 with a b.p. of 71° at 13 mm.

n_D^{20} 1.4539; d_4^{20} 0.9787; MR_D 41.11; calculated 40.45.
0.2042 g substance: 0.1939 g AgCl. Found %: Cl 23.6. $C_7H_{13}OCl$. Calculated %: Cl 23.9.

The residue consisted of a large quantity of high-boiling fractions plus tar.

Addition of alpha chloroethyl ethyl ether to butadiene. In this reaction we used 49 g of butadiene, 98 g of chloroethyl ethyl ether, and 1.5 g of pulverized zinc chloride. The procedure used in the reaction resembled that described for the preceding test. Repeated fractionations of the reaction products with a Widmer dephlegmator yielded 38.5 g of 2-ethoxy-4-chlorohexene-5 with a b.p. of 51-52° at 8 mm.

n_D^{20} 1.4334; d_4^{20} 0.9316; MR_D 45.38, calculated 45.07.
0.1990 g substance: 0.1718 g AgCl. Found %: Cl 21.4 $C_8H_{15}OCl$. Calculated %: Cl 21.8.

We also secured 41.2 g of 2-ethoxy-6-chlorohexene-4 with a b.p. of 71-72° at 10 mm.

n_D^{20} 1.4470; d_4^{20} 0.9535; MR_D 45.53; calculated 45.07.
0.1972 g substance: 0.1706 g AgCl. Found %: Cl 21.4. $C_8H_{15}OCl$. Calculated %: Cl 21.8.

The residue consisted of high-boiling fractions plus tar.

Addition of alpha chloroethyl n-butyl ether to butadiene. We used 42 g of butadiene, 104 g of alpha chloroethyl n-butyl ether, and 1.47 g of zinc chloride in this reaction. The reaction and the processing and fractionation of the reaction mixture, performed as in the preceding tests, yielded 24.9 g of 2-butoxy-4-chlorohexene-5 with a b.p. of 76-78° at 7 mm.

n_D^{20} 1.4382; d_4^{20} 0.9174; MR_D 54.52; calculated 54.31.
0.1990 g substance: 0.1480 g AgCl. Found %: Cl 18.4. $C_{10}H_{19}OCl$. Calculated %: Cl 18.6.

We also secured 34.2 g of 2-butoxy-6-chlorohexene-4 with a b.p. of 97-99° at 6 mm.

n_D^{20} 1.4510; d_4^{20} 0.9353; MR_D 54.84; calculated 54.31.
0.2049 g substance: 0.1507 g AgCl. Found %: Cl 18.2. $C_{10}H_{19}OCl$. Calculated %: Cl 18.6.

Action of KOH upon 2-methoxy-6-chlorohexene-4 dissolved in ethyl alcohol. 12 grams of KOH was dissolved in 160 g of ethyl alcohol, and 27 g of 2-methoxy-6-chlorohexene-4 was added to the resulting solution. An abundant precipitate of potassium chloride was thrown down within a few minutes, after which the reaction mixture was heated for two hours on a water bath. Then the alcohol was driven off, and the residue left in the flask treated with water and extracted with ether. After the ether layer had been dried and the ether driven off, the residue was fractionated in vacuo, yielding 18.2 g of 2-methoxy-6-ethoxyhexene-4 with a b.p. of 65-68° at 7 mm.

n_D^{20} 1.4304; d_4^{20} 0.8739; MR_D 46.77; calculated 46.35.
0.12 g substance: 0.3202 g CO_2; 0.1273 g H_2O. Found %: C 67.95; H 11.08. $C_9H_{18}O_2$.
Calculated %: C 68.25; H 11.39.

Action of KOH upon 2-methoxy-4-chlorohexene-5 dissolved in ethyl alcohol. 14 grams of KOH was dissolved in 160 g of ethyl alcohol, and then 30 g of 2-methoxy-4-chlorohexene-5 was gradually added. The reaction mixture was heated on a water bath for four hours. After the alcohol had been driven off, the residue was treated with water and extracted with ether. The alcoholic distillate was likewise treated with water and extracted with ether. The ether extracts were combined and dried over calcium chloride, after which the ether was driven off, and the residue fractionated in vacuo with a Widmer dephlegmator. This yielded 8.5 g of 2-methoxyhexadiene-3,5 with a b.p. of 60-61° at 93 mm.

n_D^{20} 1.4465; d_4^{20} 0.8132; MR_D 36.76; calculated 35.12; exaltation 1.6.
0.1258 g substance: 0.3446 g CO_2; 0.1162 g H_2O. Found %: C 74.76; H 10.35. $C_7H_{12}O$.
Calculated %: C 75.00; H 10.70.

We also recovered a mixture of ethers.

Action of maleic anhydride upon 2-methoxyhexadiene-3,5. 2.6 grams of 2-methoxyhexadiene-3,5 and 2.27 g of maleic anhydride were placed in a small round-bottomed flask. When the flask was gently heated over the flame of an alcohol lamp, a violent reaction set in, the temperature of the reaction mass rising to 170°. Fractionation of the reaction mixture yielded 2.7 g of an addition product with a b.p. of 168-170° at 8 mm,

n_D^{20} 1.4873.
0.1052 g substance: 0.2418 g CO_2; 0.0600 g H_2O. Found %: C 62.72; H 6.38. $C_{11}H_{14}O_4$.
Calculated %: C 62.85; H 6.67.

TABLE 1

Time from start of isomerization, days	2-Methoxy-4-chlorohexene-5						2-Methoxy-6-chlorohexene-4	
	0.2% $ZnCl_2$ (0.0022 mole)		0.6% $ZnCl_2$ (0.0066 mole)		1.12% $ZnCl_2$ (0.012 mole)		1.12% $ZnCl_2$ (0.012 mole)	
	n_D^{20}	% of chloride isomerized	n_D^{20}	% of chloride isomerized	n_D^{20}	% of chloride isomerized	n_D^{20}	% of chloride isomerized
1	–	–	1.4393	25.2	1.4435	45.2	–	–
4	–	–	1.4421	37.8	1.4464	60.5	–	–
9	1.4363	10.0	1.4441	48.4	1.4475	66.3	1.4532	3.6
23	1.4378	15.2	1.4461	58.9	–	–	–	–
33	1.4388	20.5	1.4472	64.7	1.4486	72.1	1.4525	7.3
56	1.4411	32.6	1.4484	71.0	1.4500	79.4	–	–
77	1.4428	41.5	1.4492	75.2	1.4509	84.2	1.4525	7.3
120	1.4451	53.6	1.4506	82.6	1.4520	90.0	1.4525	7.3

TABLE 2

Time from start of isomerization, days	0.49% $ZnCl_2$		1.23% $ZnCl_2$	
	n_D^{20}	% of chloride isomerized	n_D^{20}	% of chloride isomerized
1	1.4364	7.9	1.4388	20.5
3	1.4371	11.5	1.4391	22.1
4	1.4373	12.6	1.4394	23.6
6	1.4375	13.6	1.4396	24.7
14	1.4380	16.3	1.4402	27.8

Catalytic isomerization of the methoxychlorohexenes. In our study of catalytic isomerization we used isomeric methoxychlorohexenes with the following constants: 2-methoxy-4-chlorohexene-5 with a b.p. of 50° at 13 mm; n_D^{20} 1.4349; d_4^{20} 0.9554 and 2-methoxy-6-chlorohexene-4 with a b.p. of 71° at 13 mm; n_D^{20} 1.4539; d_4^{20} 0.9787. Isomerization was effected in the presence of zinc chloride by the method described in our previous papers [6,7]. The percentage of isomeric chlorides in the reaction mixtures was calculated from the measurements of the refractive index. The first series of tests was run at +20°; the results are listed in Table 1.

The catalytic isomerization of 2-methoxy-4-chlorohexene-5 in the presence of zinc chloride at 0° is shown in Table 2.

SUMMARY

1. A study has been made of the addition of α-chloroethyl methyl, α-chloroethyl ethyl, and α-chloroethyl butyl ethers to butadiene, the corresponding 1,2 and 1,4 addition products being isolated and identified.

2. A study has been made of the catalytic isomerization of the isomeric methoxychlorohexenes in the presence of zinc chloride. 90-93% of 2-methoxy-6-chlorohexene-4 is in equilibrium with 7-10% of 2-methoxy-4-chlorohexene-5.

3. The order of addition of alpha chloroethyl methyl ether to butadiene has been determined. 65-75% of the haolgen ether is added at the 1,2 position, with 25-35% added at the 1,4 position.

4. The existing notions of the mechanisms involved in the addition of halogen derivatives to butadiene are subjected to a critical review. The opinion is expressed that the alpha halogen ethers and other halogen derivatives are added to butadiene ionnomolecularly rather than ionically.

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Received October 6, 1950

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* See Consultants Bureau English Translation, p. 1173.

** See Consultants Bureau English Translation, p. 1037.

*** See Consultants Bureau English Translation, p. 241.

**** See Consultants Bureau English Translation, pp. 67 and 1025.

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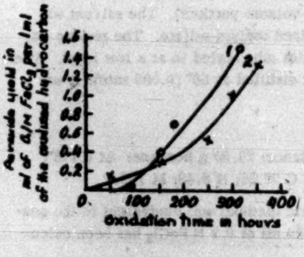
n-BUTYLBENZENE PEROXIDE

K. I. Ivanov, V. K. Savinova, and V. P. Zhakhovskaya

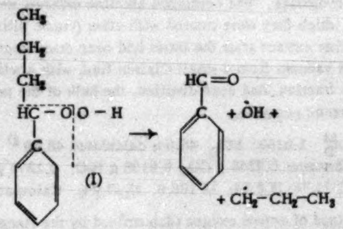
Of the peroxides of derivatives of the higher monoalkylbenzenes, only two tertiary hydroperoxides are known up to the present time, namely: isopropylbenzene hydroperoxide [1] and 2-phenylbutane hydroperoxide [2], which are produced fairly readily by oxidizing the respective hydrocarbons containing tertiary carbon atoms in the side chain at the alpha position with molecular oxygen.

In this connection we were interested in exploring the reaction with oxygen of benzene hydrocarbons containing an unbranched side chain, which do not possess readily peroxidized aliphatic tertiary C—H groups, and in studying the structure of the peroxides initially formed in this reaction. With this in mind we undertook the oxidation of n-butylbenzene by bubbling oxygen through it at 80° and irradiating it with ultraviolet light. Though this hydrocarbon begins to oxidize in the pure state under these conditions much later than secondary butylbenzene (it exhibits a long induction period), the accumulation of the peroxide takes place more rapidly later on (see figure). Adding some of the already oxidized hydrocarbon or some of its peroxide speeds up the oxidizing process considerably.

The peroxide formed as the initial product in the photooxidation of n-butylbenzene is a hydroperoxide with an OO—H group attached to the alpha carbon atom in the side chain (I).



Accumulation of peroxides in the oxidation of normal (I) and secondary (II) butylbenzenes in ultraviolet light at 80°.



The hydroperoxide of n-butylbenzene (1-phenylbutane hydroperoxide-1) is a colorless, transparent, rather viscous liquid that is readily soluble in organic solvents and nearly insoluble in water. The hydroperoxide of n-butylbenzene reacts even with a dilute aqueous solution of sodium hydroxide, yielding a sodium salt. When a hydrocarbon solution of the peroxide is treated with a concentrated (30%) solution of sodium hydroxide, the salt is precipitated as white crystals, which quickly deliquesce in air. When an aqueous solution of the salt is decomposed in the cold by dilute mineral acids, we recover the initial hydroperoxide.

When the hydroperoxide is boiled with a solution of ferrous sulfate, it is decomposed, yielding benzaldehyde, thus proving that the OOH group is at the alpha position. The hydroxyl and propyl radicals arising thereby (see the equation) can apparently condense partially, giving rise to n-propyl alcohol, and partially react in other ways.

The results of our investigation of the structure of the peroxide produced in the autocondensation of n-butylbenzene indicate that the molecular oxygen is first added to the α-carbon atom of the higher monoalkylbenzenes even when the latter is not a tertiary carbon atom but a much less reactive secondary one.

EXPERIMENTAL

Preparation of n-butylbenzene. 300 ml of anhydrous ethyl ether was added to 100 g of finely cut metallic sodium in a 1-liter Pyrex flask fitted with a reflux condenser, and then a mixture of 240 g of n-butyl bromide and 240 g of bromobenzene, both previously refined by fractionation and drying, was added. The reaction was violent at first, so that the flask had to be cooled. After 15-20 hours a straight condenser was substituted for the reflux one, and the ether was first driven out of the reaction mixture (on a water bath), after which a 170-185° fraction was collected. This fraction was then fractionated with a Hahn dephlegmator. The 181-184° fraction collected was redistilled at reduced pressure into a one-meter heated column, with an efficiency of 16 theoretical plates, and a packing consisting of cylinders 2 mm in diameter and 3 mm high, twisted from copper screening. The principal fraction, boiling at 70-70.5° at 10 mm, was pure n-butylbenzene with a d_4^{20} 0.8609 and n_D^{20} 1.4900 (b.p. 184° at atmospheric pressure).

Synthesis of n-butylbenzene peroxide. The normal butylbenzene was oxidized in two quartz flasks, fitted with reflux condensers and each containing 180 g of the hydrocarbon, by bubbling oxygen through at the rate of 5 ml per min. and at 80° while the flasks were irradiated by the ultraviolet light of a mercury lamp. After 440 hours of treatment the amount of active oxygen in the oxidized product was equivalent to 1.4-1.6% of the peroxide.

The peroxide concentrate (60 g) left after the bulk of the unreacted hydrocarbon had been driven off in vacuo (about 5/6 of the total volume) was an intense yellow. It was agitated twice with 8 ml and twice with 4 ml of a 0.25% aqueous solution of NaOH and twice with 4 ml of water to eliminate the coloring impurities. Then the decolorized product was treated five times in a separatory funnel with 0.25 its volume of a 7% aqueous solution of sodium hydroxide. The combined alkaline extracts were chilled to 0° and neutralized with 10% sulfuric acid, after which they were treated with ether (twice with 0.25 volume portions). The solvent was driven out of the ether extract after the latter had been dried over calcined sodium sulfate. The residue was fractionated at high vacuum from a small Claisen flask with a wide outlet tube sealed in at a low level. After the small overhead fraction had been distilled, the bulk of the product distilled at 56° (0.006 mm); it was the pure n-butylbenzene peroxide.

d_4^{20} 1.016; n_D^{20} 1.5103. MR_D 48.94; calculated 48.49 1)
0.2764 g substance: 0.7246 g CO_2; 0.2108 g H_2O. 0.1276 g substance; 21.90 g benzene: Δt 0.178°.
Found %: C 71.70; H 8.54; M 166.9. $C_{10}H_{14}O_2$. Calculated %: C 72.26; H 8.48; M 166.2

The percentage of active oxygen (determined by the stannometric method) was equivalent to the consumption of 19.7 ml of 0.1N $FeCl_3$ per millimole. For $C_{10}H_{13}-OO-H$ 20 ml of 0.1 N $FeCl_3$ has been calculated per millimole.

The hydroperoxide of n-butylbenzene exhibits qualitative reactions for active oxygen (evolution of iodine from a solution of potassium iodide, coloring a thiocyanate solution) and for a hydroperoxide group with zinc tetraacetate.

Decomposition of n-butylbenzene peroxide. 0.6 g of the hydroperoxide was boiled for 4 hours with 15 ml of a 25% aqueous solution of $FeSO_4 \cdot 7H_2O$ in a small flask fitted with a reflux condenser. After standing overnight, the product was fractionated with steam. A heavy yellow liquid (0.3 g), exhibiting the characteristic odor of bitter almonds and consisting of benzaldehyde, as proved by the following tests, accumulated in the distillate beneath an upper aqueous layer.

1. 6 ml of a solution of p-nitrophenylhydrazine (1 g of p-nitrophenylhydrazine in 50 ml of 50% acetic acid) was added to 0.1 g of the liquid. The abundant orange precipitate of the hydrazone that settled out at once was filtered out on a Schott filter, washed with water, twice recrystallized from alcohol, and dried at 80°; m.p. 189°. Its mixed melting point with the specially prepared p-nitrophenylhydrazone of benzaldehyde (m.p. 192°) was 190°.

2. 0.1 gram of the liquid was added to a solution of 0.3 g of dimedon in 15 ml of 50% ethyl alcohol. The white precipitate that settled out 6 hours later was twice recrystallized from dilute alcohol. M.p. 193°. The mixed melting point with the benzaldehyde (m.p. 192°) derivative prepared in the same way was 193°.

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1) By the method described previously [3].

SUMMARY

It has been shown that the photooxidation of n-butylbenzene by oxygen at 80° results in the formation of a hydroperoxide with an —OOH group attached to the alpha carbon atom in the side chain. The hydroperoxide of n-butylbenzene has been isolated and identified.

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Received August 4, 1950

METHODS OF PRODUCING DIALKYL PEROXIDES

TETRALYL ETHYL PEROXIDE AND PHENYL ISOPROPYL ETHYL PEROXIDE

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Our inadequate knowledge of the dialkyl peroxides, especially the peroxides with mixed hydrocarbon radicals, is due to the imperfection of the methods hitherto employed in their preparation, so that the number of compounds of this type known up to the present time is extremely limited.

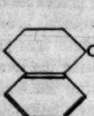
The method of alkylating hydrogen peroxides with dialkyl sulfates, as employed by Hock and Lang [1], for example, in synthesizing tetralyl methyl, cyclohexenyl methyl, p-menthenyl methyl, and hydrindenyl methyl peroxides, always involves the partial disintegration of the initial hydroperoxide by the reagent. This diminishes the yield of the synthesized peroxide and entails the difficult purification of the latter to eliminate the resultant decomposition products. Moreover, the distillation of the reaction product required during the course of the synthesis then involves the danger of the explosive decomposition of the peroxide produced, due to the presence of even traces of the unreacted dialkyl sulfate.

In our search for better methods of synthesizing dialkyl peroxides, we have made use of the action of alkyl halides upon alkaline salts of the hydrogen peroxides:

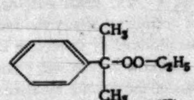
$$R{-}OO{-}Na + HalR_1 = R{-}OO{-}R_1 + NaHal.$$

This method proved to be free of the disadvantages enumerated above and to be quite convenient for the synthesis in particular, of the alkyl derivatives of alpha aryl-substitution derivatives of alkyl hydrogen peroxides, which readily form alkaline salts that in many cases can be isolated in the pure crystalline state without difficulty. We have worked out the conditions required for this synthesis; in particular, we have found that the reaction proceeds smoothly at room temperature in methanol, which satisfactorily dissolves both the initial sodium salts of the hydrogen peroxides and the alkyl halides. The latter must be used in excess to ensure a high yield of the synthesized peroxide. The NaHal produced in the reaction is precipitated under the given conditions. The resulting $R{-}OO{-}R_1$ peroxide is recovered by diluting the filtrate with water and is refined by distillation or other methods.

Starting with tetralin hydrogen peroxide and isopropylbenzene hydrogen peroxide, we produced tetralyl ethyl peroxide (I) and phenyl isopropyl ethyl peroxide (II), hitherto not described in the literature, as far back as 1948 [2]:



(I)

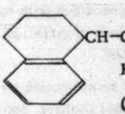


(II)

In the pure state, both of these compounds are colorless liquids with the acrid odor that is characteristic of organic peroxides, which do not solidify when chilled to -18°. They exhibit intensive qualitative reactions for peroxide oxygen, though they do not react with lead tetraacetate (proof that no hydrogen peroxide group is present). Both of the peroxides are fairly inert chemically, as is typical of H_2O_2 derivatives in which both of the hydrogen atoms have been replaced by hydrocarbon radicals. Only part of their active oxygen, namely, 19.2% in the tetralyl ethyl and 70% in the phenyl isopropyl ethyl peroxides, can be detected iodometrically (even in the severe conditions we have worked out especially[1]). The stannometric method yields results that are still lower for the second of these compounds (22% for the tetralyl ethyl peroxide and 30% for the phenyl isopropyl ethyl peroxide).

Tetralyl ethyl peroxide (d_4^{20} 1.0696; n_D^{20} 1.5321) is distinguished from the phenyl isopropyl ethyl peroxide (b.p. 41.5° at 0.03 mm; d_4^{20} 0.9842; n_D^{20} 1.4960) by its higher viscosity. It also has a higher boiling point, though it is less stable at higher temperatures, so that it cannot be distilled without partial decomposition, even at high vacuum (0.005 mm).

Reduction of both peroxides with hydrogen in statu nascendi confirmed their structures by the production of the following: the first one yielded ethyl alcohol and alpha tetralol (Formula III), while the second yielded ethyl alcohol and dimethylphenylcarbinol (Formula IV).



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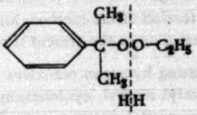

(IV)

EXPERIMENTAL

Tetralyl Ethyl Peroxide. Synthesis. 5 ml of a 37% aqueous solution of NaOH was added at 0°, with vigorous stirring, to 12 g of pure (m.p. 56°) tetralin hydrogen peroxide (prepared by catalytically oxidizing tetralin by the method developed by one of the present authors together with V. Savinova and E. Mikhailova [3]), dissolved in 100 ml of benzene that contained no thiophene. The precipitated salt was filtered out at once and washed with benzene on a Buchner funnel. The resulting sodium salt of tetralin hydrogen peroxide was pressed out between sheets of filter paper (yield of about 8 g) and then dissolved in 150 ml of methanol that had been previously dried with calcined sodium sulfate and distilled. The solution, which was slightly cloudy, was allowed to stand in the dark at room temperature for 40 hours after 35 g (a 6.5-fold excess) of anhydrous ethyl bromide had been added to it. After the precipitated NaBr had been filtered out, the solution was diluted with 1.5 volumes of distilled water. The small lower layer that separated out, consisting of a solution of the peroxide in an excess of ethyl bromide, was separated from the upper water-alcohol layer, which was triply extracted with 0.5-volume portions of distilled diethyl ether. The lower layer was combined with the ether extracts of the upper layer, washed with distilled water, and thoroughly dried with calcined sulfate (the latter being frequently replaced by fresh batches). Then the ether and the ethyl bromide were driven out of the mixture at reduced pressure on a water bath. The residue (totaling some 5 g) was kept for two hours at 1 mm pressure and room temperature. The 14 grams of the crude product (n_D^{20} 1.5480) accumulated in this manner was freed of the tetralone and other impurities it contained by dissolving it in the minimum quantity of 88% methanol and triple extraction with 0.3-volume portions of petroleum ether with a b.p. below 63°. The combined petroleum ether extracts were washed with 0.3 volume of water and dried with calcined sulfate, after which the solvent was driven off in vacuo (at room temperature). Repurification by the procedure outlined yielded 6.5 g of a residue with n_D^{20} 1.5328. Final refining (dissolution in 100 ml of 76% aqueous acetone and a single extraction with 50 ml of petroleum ether) yielded 5.5 g of a product with n_D^{20} 1.5320. The product (which was faintly yellowish) was decolorized by dissolving it in 6 ml of methanol and agitating the solution for 20 minutes with 0.6 g of finely pulverized activated charcoal. The whole was filtered after one hour had passed, and the solvent was driven out of the filtrate by distillation in vacuo. The residue was a colorless, transparent, viscous liquid that did not solidify when chilled to -18°; it was tetralyl ethyl peroxide: d_4^{20} 1.0694; n_D^{20} 1.5321; δ (specific dispersion) = $\frac{n_F - n_C}{d} \cdot 10^4 = 145.9$.

0.2372 g substance: 0.6542 g CO_2; 0.1806 g H_2O. 0.2104 g substance; 20.772 g benzene: Δt 0.272°. Found %: C 75.22; H 8.52; O (by difference) 16.26; M 190.0. $C_{12}H_{16}O_2$. Calculated %: C 74.98; H 8.39; O 16.64; M 192.2.

Tetralyl ethyl peroxide exhibits a strong qualitative reaction for active oxygen (evolution of iodine from a neutral KI solution; coloring of a thiocyanate solution). Its reaction for a hydrogen peroxide group with lead tetraacetate is negative. A drop of the peroxide burns in a Bunsen burner flame with a gentle smoky flame.

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[1] Heating a sample of the peroxide with KI and hydrochloric acid in alcoholic solution for two hours to 50° in an atmosphere of CO_2 prior to titration with hyposulfite.

When tetralyl ethyl peroxide is heated above 80°, it decomposes, giving rise to liquid and gaseous products. It distills (with partial decomposition) at 55° at 0.005 mm (water bath warmed to 82°).

Tetralyl ethyl peroxide is soluble in ether, benzene, petroleum ether, methanol, ethyl alcohol, acetone, and CCl_4; it is insoluble in water.

Reduction. A small amount of distilled water was poured into 1.1 g of the peroxide distilled in 27 ml of concentrated acetic acid(until turbidity appeared, which disappeared upon heating). After 1 g of zinc dust was added, the mixture was refluxed for 30 minutes in a small flask fitted with ground-glass reflux condenser. Then the liquid in the flask, which did not exhibit a qualitative reaction for active hydrogen, was carefully decanted from the unreacted zinc and neutralized with 25% KOH.

The resultant precipitate was filtered out, and the lightest portion (3 ml) of the filtrate was driven off into a three-bulb Glinsky dephlegmator. The residue was treated twice with diethyl ether. The ether extract was washed with water and dried with calcined sulfate, and then the solvent was driven off. The remaining oily, yellowish liquid (0.6 g) was refluxed at 80-90° for 2 hours with 0.4 g of phenyl isocyanate. Then the mixture was steam-distilled to drive off the volatile components, the residue being extracted with petroleum ether. Evaporation of the solvent yielded white crystals, whose m.p. was 120.8° after double recrystallization from petroleum ether. The mixed melting point with the phenylurethane of specially synthesized alpha tetralol (m.p. 121.0°) was 120.8°.

The volatile reduction products were analyzed by treating a new portion of the peroxide (0.7 g) with hydrogen in status nascendi in the same vessel, but this time the upper end of the reflux condenser was connected to a trap (Petri bottle) containing 2 ml of distilled water, and the mixture with 0.7 g of zinc dust and 25 ml of 7% sulfuric acid (instead of acetic acid) was heated for 18 minutes. The reaction product, which was decanted from the zinc and then neutralized, was distilled (with a Glinsky three-bulb dephlegmator), the lightest portion (3 ml) being driven off. The water in the trap was added to the resultant aqueous distillate, the water-insoluble products were removed by extraction with petroleum ether, 0.5 g of p-nitrobenzoyl chloride and 3 ml of benzene were added, and the mixture was vigorously agitated with 0.9 ml of 20% aqueous NaOH. The upper (benzene) layer that collected upon standing was separated. When the benzene was allowed to evaporate from a watch glass, what was left was ethyl p-nitrobenzoate, which crystallized upon chilling; its m.p. was 55.5° after double recrystallization from petroleum ether. The mixed melting point with pure ethyl p-nitrobenzoate (m.p. 56°) was 55.7°.

Phenyl Isopropyl Ethyl Peroxide. Synthesis. 20.9 g of pure isopropylbenzene hydrogenperoxide, n_D^{20} 1.5244 (prepared by the thermal oxidation of isopropylbenzene [4]), was dissolved in 160 ml of benzene. The solution was placed in a three-necked flask fitted with a thermometer and a stirrer and chilled to +2° and then stirred vigorously while 23 g of similarly chilled 30% aqueous NaOH was gradually added (without allowing the temperature to rise above 8°). The precipitated sodium salt of isopropylbenzene hydrogenperoxide was filtered out in a Buchner funnel, washed with benzene, and dried between sheets of filter paper. The resultant salt (totaling about 36 g) was dissolved in 400 g of pure anhydrous methanol, and 40 g (more than 100% excess) of dried ethyl bromide was added. After the mixture had stood for 40-60 hours in the dark at room temperature, the precipitated crystals of NaBr were filtered out, and 15 volumes of water were added to the filtrate. The resultant lower layer was separated, and the upper layer was triple-extracted with 0.3-volume portions of diethyl ether. The ether extracts were washed with distilled water, combined with the lower layer, and then dried for 3 days with calcined sulfate (the sulfate being replaced twice by fresh batches). The barely yellowish, viscous liquid (14.2 g)1) that remained after the ether and ethyl bromide had been driven off in a vacuum established by a water pump was fractionated at high vacuum from a Claisen flask made of molybdenum glass, fitted with

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1) We have observed that in some instances the reaction is not complete, the product containing some isopropyl hydrogen peroxide (which arises, apparently, as the result of hydrolysis of the unreacted salt), as evidenced by its higher refractive index and its ability to react weakly with lead tetraacetate. The product can be freed of its hydrogen peroxide by treating its (1:4) benzene solution in the cold two or three times with a few ml of a 30% NaOH solution, and then processing it 5 or 6 times with half its volume of a 7% NaOH solution. Then it is washed with water and dried, the solvent is driven off, and the residue is fractionated at a high vacuum as described above.

a wide outlet tube (the water-bath temperature not exceeding 54°). After the first runnings had been distilled, the bulk of the product distilled at constant temperature. This principal fraction (11 g), which had a b.p. of 41.5° at 0.03 mm, was a colorless, transparent, mobile liquid that did not solidify when chilled to -18° and consisted of phenyl isopropyl ethyl peroxide: d_4^{20} 0.9842; n_D^{20} 1.4960; (specific dispersion) = δ

$$= \frac{n_F - n_C}{d} \cdot 10^4 = 134.7.$$

0.1962 g substance: 0.5276 g CO_2; 0.1586 g H_2O. 0.1248 g substance; 20.45 g benzene: Δt 0.174°. Found %: C 73.34; H 9.05; O (by difference) 17.61; M 178.9. $C_{11}H_{16}O_2$. Calculated %: C 73.30; H 8.95; O 17.75; M 180.2.

Phenyl isopropyl ethyl peroxide exhibits strong qualitative reactions for active oxygen (liberating iodine from a neutral KI solution and coloring a thiocyanate solution). Its reaction with lead tetraacetate is negative, evidence that no hydrogen peroxide group is present. When a drop of the peroxide is burned, it burns with a quiet, smoking flame.

Phenyl isopropyl ethyl peroxide is a fairly stable compound.

A sample of the pure peroxide suffered hardly any changes in its constants (specific gravity and refractive index) when kept for 19 months in a glass vessel at room temperature in our laboratory.

Phenyl isopropyl ethyl peroxide is soluble in ether, benzene, petroleum ether, methanol, ethyl alcohol, acetone, and CCl_4; it is insoluble in water.

Reduction. Two grams of the peroxide was dissolved in 54 ml of concentrated acetic acid. Distilled water was gradually added to the solution until a turbidity that vanishes upon heating appears. After 2.4 g of zinc dust had been added to the mixture, it was heated for 25 minutes in a flask fitted with a ground-glass reflux condenser. After a check for the absence of any reaction for active oxygen, the liquid was decanted from the unreacted zinc dust in the flask and neutralized with a 20% solution of NaOH. After the precipitate thrown down had been filtered out, the filtrate was treated twice with diethyl ether. The ether extract was washed with water and dried with calcined sulfate, after which the solvent was driven off on a water bath. The residue (0.6 g) was distilled in vacuo from a miniature Wurtz flask. The bulk of the distillate, which had a boiling point of 68° at 4 mm, crystallized. The melting point of the crystals was 26° after they had been pressed out between sheets of filter paper. The mixed melting point with dimethylphenylcarbinol (m.p. 26.5°) synthesized by the Klages method [5] was 26°.

The volatile products of reduction were analyzed by reducing a new portion of the peroxide (1.0 g) with zinc in the presence of sulfuric acid, as described above for tetralyl ethyl peroxide. The first (light) fraction secured in distilling the reduction product was treated with p-nitrobenzoyl chloride, yielding a p-nitrobenzoate, which had a m.p. of 56°. The mixed melting point with the ethyl ester of p-nitrobenzoic acid (m.p. 57°) was 57°.

SUMMARY

1. A method has been suggested and worked out to synthesize dialkyl peroxides by reacting alkaline salts of the hydrogen peroxides with alkyl halides dissolved in methanol.

2. Tetralyl ethyl and phenyl isopropyl ethyl peroxides, hitherto not described in the literature, have been synthesized and identified.

3. The structure of these peroxides has been established.

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Received August 4, 1950.

THE POLYMERIZATION OF RING-SUBSTITUTED HALOGEN DERIVATIVES OF STYRENE

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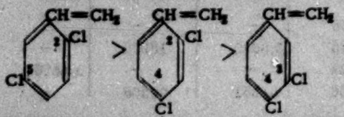
There are no systematic investigations of the physicochemical properties and the polymerizability of the dichlorostyrenes in the literature, despite the practical and theoretical interest attaching to such a study. The papers by Rutkovsky [1] and Marvel [2] contain very brief information in the properties of polydichlorostyrenes. We set as our goal the synthesis and the study of the polymerizability of three dichlorostyrenes: 2,5-dichlorostyrene, 2,4-dichlorostyrene, and 3,4-dichlorostyrene, as we had previously shown [3] that the isomers of halogen-substituted styrenes exhibit different polymerization rates. The constants of the dichlorostyrenes we synthesized are given in Table 1.

TABLE 1

No.	Name	Boiling point	Specific gravity at 20°
1	2,5-Dichlorostyrene	90-94° (5 mm) 72-73 (2 mm)	1.246
2	2,4-Dichlorostyrene	80-81 (6 mm)	1.249
3	3,4-Dichlorostyrene	92 (6 mm)	1.256

The samples tested contained 99.1-99.5% of the monomer. We studied the polymerization of the dichlorostyrenes at 75, 100, and 125° with no catalysts present, under the same conditions as those reported in our first report [3]. Our results indicate (see graphs) that introducing two chlorine atoms into the styrene's benzene ring increases the rate of polymerization substantially. When we compare the polymerization rates of dichlorostyrenes and monochlorostyrenes [3], we see that the introduction of a second chlorine atom into the styrene's benzene ring increases the polymerization rate by a factor of three, on the average. Moreover, the isomerism of the basic molecules of the halogen-substituted styrenes is of tremendous importance in this connection. In the monochlorostyrenes, the ortho isomer exhibits the higher polymerization rate, while in the dichlorostyrenes, the 2,5-dichlorostyrene exhibits the highest polymerization rate and the 3,4-dichlorostyrene the lowest rate. At 100°, for example, 3 hours of polymerization yields 72.3% of the polymer of 2,5-dichlorostyrene, 64.3% of the polymer of 2,4-dichlorostyrene, and 37.3% of the polymer of 3,4-dichlorostyrene while styrene itself yields 8% of the polymer.

The dichlorostyrenes may therefore be arranged in the following series in order of increasing rate of polymerization:



If we take the mean values, we find that 2,5-dichlorostyrene is polymerized 6 times as fast as pure styrene, while 2,4-dichlorostyrene is polyermized 5 times as fast and 3,4-dichlorostyrene is polymerized 3 times as fast. 2,5-Dichlorostyrene, in turn, is polymerized twice as fast as 3,4-dichlorostyrene. The differences between the rates of polymerization of the isomeric dichlorostyrenes, on the one hand, and the isomeric ortho and para monochlorostyrenes, on the other, are indisputable evidence of the presence of a special "ortho effect" (o-chlorostyrene, 2,5-dichlorostyrene, and 2,4-dichlorostyrene), manifested not only as polymerizability but also in some other instances.

The effect of temperature upon the rate of polymerization of the dichlorostyrenes is likewise of interest. At 75°, for example, 58% of 2,5-dichlorostyrene is converted into a polymer, within 10 hours, whereas the same result is achieved at 100° within 2 hours, and within less than 30 minutes at 125°.

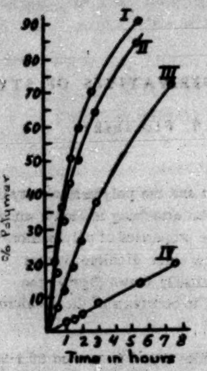


Fig. 1. Polymerization of dichlorostyrenes at 100°. I) 2,5-dichlorostyrenes; II) 2,4-dichlorostyrene; III) 3,4-dichlorostyrene; IV) styrene.

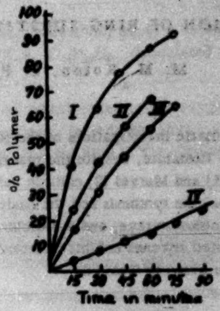


Fig. 2. Polymerization of dichlorostyrenes at 125°. I) 2,5-dichlorostyrene; II) 2,4-dichlorostyrene; III) 3,4-dichlorostyrene; IV) styrene.

TABLE 2
Molecular Weights of Polydichlorostyrenes

No.	Temperature	Time, hours	2,5-Dichlorostyrene		2,4-Dichlorostyrene		3,4-Dichlorostyrene	
			n_{sp}	Molecular weight	n_{sp}	Molecular weight	n_{sp}	Molecular weight
1	75°	5	1.1990	66611	0.4623	25683	–	–
2		7	1.2070	67055	0.4929	27383	–	–
3		10	1.5331	85172	0.5271	29283	–	–
4	100	1.5	1.1077	61538	0.4758	26433	–	–
5		3.5	1.1479	63772	0.5015	27861	0.5454	30300
6		5.5	1.1607	64483	0.5659	31438	0.5531	30727
7		7.5	1.3070	72611	0.6189	34383	0.5645	31361
8	125	0.25	0.9352	51955	–	–	–	–
9		0.50	1.0515	58416	0.3042	16900	–	–
10		0.75	0.9220	51222	–	–	0.4696	26088
11		1.00	0.9066	50366	0.4051	22505	–	–

Notes. 1. The molecular weights of the polydichlorostyrenes were determined after they had been precipitated with methanol from benzene solutions and dried to constant weight.

2. The molecular weights of the polymers of the 2,5- and 2,4-dichlorostyrenes were determined in benzene solutions, while that of the polymer of 3,4-dichlorostyrene was determined in a chloroform solution.

3. The equation $n_{sp} = K_m \underline{CM}$, where $K_m = 1.80 \cdot 10^{-4}$, was used in our calculations.

Measurements of the molecular weights of the polydichlorostyrenes (Table 2) indicate that the polymers of 2,5-dichlorostyrene have the highest molecular weight, of the order of 60,000 to 85,000, while the molecular weights of the polymers of the 2,4- and 3,4-dichlorostyrenes range from 26,000 to 31,000.

The polymers of the dichlorostyrenes are transparent and colorless and have a rather high softening point (160-180° in a capillary). The polymers of the 2,5- and 2,4-dichlorostyrenes are soluble in benzene, toluene, xylene, carbon tetrachloride and chloroform, while the polymer of 3,4-dichlorostyrene is soluble only in chloroform.

Study of the kinetics of polymerization of the dichlorostyrenes indicates that this process is a first-order reaction.

We calculated the activation energies for the isomeric dichlorostyrenes, as shown in Table 3.

TABLE 3

No.	Name	Activation energy Cal/mole
1	2,5-Dichlorostyrene	16.97
2	2,4-Dichlorostyrene	15.55
3	3,4-Dichlorostyrene	15.56
4	Styrene	20.13

These figures indicate that the introduction of two chlorine atoms into the styrene benzene ring diminishes the activation energy of the polymerization process.

SUMMARY

1. A study has been made of the polymerization of the 2,5-, 2,4-, and 3,4-dichlorostyrenes at 75, 100, and 125° with no catalysts present.

2. The introduction of two chlorine atoms into styrene's benzene ring greatly increases the polymerization rate of the substitution derivatives of styrene.

3. The highest polymerization rate is exhibited by 2,5-dichlorostyrene, with 3,4-dichlorostyrene having the lowest rate.

4. The introduction of chlorine atoms into styrene's benzene ring diminishes the activation energy of the polymerization process.

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Received July 17, 1950

SYNTHESIS OF TRIARYL PHOSPHINES AND TRIARYL PHOSPHINOXIDES USING ORGANOLITHIUM COMPOUNDS

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The only carbocyclic phosphorus compounds known at the present time with the phosphorous atom attached to the aromatic ring are derivatives of benzene and naphthalene, no more complex compounds in which the condensed systems contain more than two benzene rings being known.

Setting as our objective the production of organophosphorous compounds of polycyclic hydrocarbons, we undertook a systematic testing of methods of synthesizing phosphorous derivatives; the example of anthracene convinced us of their unsuitability for use with polycyclic systems. We found, for instance, that anthracene does not react with phosporous trichloride in the presence of aluminum chloride; anthracene reacts with phosphorus pentachloride to constitute chlorine derivatives rather than phosphorus compounds [1], as might have been expected by analogy with unsaturated hydrocarbons; in this case, the method of synthesizing alkyl and aryl methylphosphinic acids developed by A.E. Arbuzov [2] is obviously unusable because of the low mobility of a halogen atom in halogen derivatives of aromatic hydrocarbons; and lastly, phosphorus derivatives of anthracene can not be produced by reacting an organomagnesium reagent with phosphorus trichloride [3]. We set about determining the feasibility of using lithium reagents in the synthesis of phosphorus compounds and found that they are highly effective agents for the synthesis of various classes of carbocyclic organophosphorus compounds.

The present paper describes a method of synthesizing triaryl phosphines and oxides of triaryl phosphines by means of lithium reagents, that makes it possible to synthesize compounds of this type in the tricyclic and tetracyclic series of hydrocarbons, hitherto unknown, in addition to those in the monocyclic and bicyclic series, which can be obtained by other methods of synthesis as well.

The method employed in synthesizing these groups of phosphorus compounds involves the action of organolithium compounds of aromatic hydrocarbons upon phosphorus trichloride (to produce triaryl phosphines) and upon phosphorus oxychloride (to produce triaryl phosphine oxides). The method was first tried out on the simplest types of these compounds — phenyllithium and α-naphthyllithium — after which it was applied to more complicated compounds.

Aryl lithium compounds react with phosphorus trichloride to produce triaryl phosphines as follows:

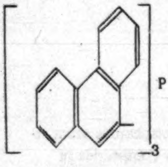
$$3ArLi + PCl_3 = Ar_3P + 3LiCl.$$

The reaction is carried out by adding an ether solution of phosphorus trichloride to an ether solution or a suspension in ether of the organolithium compound, prepared from the aryl halide and metallic lithium (for phenyllithium and α-naphthyllithium) or n-butyllithium (for the other aryl lithium compounds). In some instances the reagents were mixed together in the inverse order. When we react 3 equivalents of phenyllithium with phosphorous trichloride, we can secure 61% of the theoretical yield of triphenylphosphine. Pfeiffer [4] used an organomagnesium compound when he secured a poor yield (about 12%) of triphenylphosphine, an appreciable yield of triphenylphosphine being obtained only when an excess of phenylmagnesium bromide was employed [5].

The reaction is not as smooth when α-naphthyllithium is employed, the yield of tri-(α-naphthyl)-phosphine being only 27%. This compound has been described by Anschutz and his co-workers, who synthesized it from α-naphthylmagnesium bromide and phosphorus trichloride.

Reacting 9-phenanthryllithium with phosphorus trichloride yields tri-(9-phenanthryl)-phosphine (I), the yield being 72% of the theoretical.

We have synthesized the following derivatives of anthracene: tri-(9-anthryl)-phosphine (II) and tri-(9-bromoanthryl-10)-phosphine (III) The yield of the former from 9-anthryllithium totaled 20%; together with the phosphine we secured about the same quantity of anthracene, which is evidence of the complexity of the reaction between phosphorus trichloride and 9-anthryllithium. We synthesized the compound (III) by reacting 9-bromoanthryl-10-lithium, prepared by reacting 9,10-dibromoanthracene and phenyllithium together with PCl$_3$.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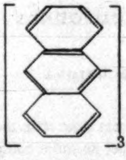
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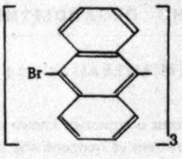
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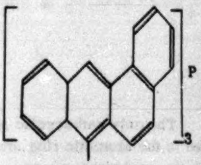

(IV)

Tri-(1,2-benzanthryl)-phosphine (IV) was synthesized similarly, the yield being 55% of the theoretical.

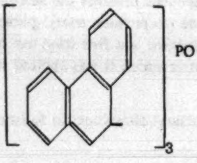
The reaction of aryl lithium compounds with phosphorous oxychloride in ether results in the formation of triaryl phosphine oxides, as follows:

$$3ArLi + POCl_3 = Ar_3PO + 3LiCl.$$

Triphenylphosphine oxide was synthesized by this method, with a yield of 65%, i.e., the same yield as when a Grignard reagent was used [6].

Tri-(α-naphthyl)-phosphine oxide, synthesized by the use of organomagnesium compounds [7] (no yield being stated), is produced by reacting α-naphthyllithium with phosphorus oxychloride, the yield being 38% of the theoretical.

A derivative of a tricyclic hydrocarbon—tri-(9-phenanthryl)-phosphine oxide—and a derivative of a tetracyclic hydrocarbon—tri-(1,2-benzanthryl)-phosphine (VI)—have been secured with satisfactory yields by this same method.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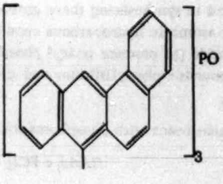
(VI)

EXPERIMENTAL

All operations with organolithium compounds were performed in a nitrogen atmosphere. A two-necked ampoule was used as the reaction vessel in all cases.

Triphenylphosphine. A solution of phenyllithium, prepared from 5 g of bromobenzene, 0.44 g of lithium, and 30 ml of absolute ether was stirred and chilled with snow and salt while 1.3 g of phosphorus trichloride diluted with 20 ml of absolute ether was added during the course of 15-20 minutes. Considerable heat was evolved, the ether solution turning yellow. The reaction mass was decomposed with water, the ether extract being separated and washed with a 10% NaOH solution and then with water, and the ether driven off. The residue, 4.6 g of an oil, crystallized when alcohol was added to it. The substance was filtered out (1.9 g; m. p. 72-74°) and crystallized from alcohol. This yielded 1.7 g of triphenylphosphine as colorless lamellae with a m.p. of 77-78°. The yield was 61.3%, based on the bromobenzene used in the reaction.

Tri-(α-naphthyl)-phosphine. A solution of α-naphthyllithium, prepared from 4 g of α-bromonaphthalene, 0.27 g of lithium, and 55 ml of absolute ether, was chilled with snow and salt and vigorously stirred while an ether solution (50 ml) of 0.8 g of phosphorus trichloride was added during the course of half an hour. No heat was evolved, and the reaction mass gradually turned a greenish-yellow. When the reaction was finished, the mixture was stirred while water was added, after which a dilute solution of alkali was added until the reaction was alkaline, and the ether extract was separated, washed with water, and dried with anhydrous sodium sulfate. The ether was driven off until the volume totaled 7-10 ml, and the precipitate was filtered out. This yielded 0.7 g (26.9%) of tri-(α-naphthyl)-phosphine with an m.p. of 276-278°. The product is slightly soluble in ordinary organic solvents and crystallizes from a large quantity of chloroform as a molecular compound with the formula of $(C_{10}H_7)_3P \cdot CHCl_3$ and an m.p. of 260-262°. After the tri-(α-naphthyl)-phosphine had been heated to 110° for several hours, it lost its solvent and had an m.p. of 276-278°, which agrees with the figure given in the literature.

Tri-(9-phenanthryl)-phosphine. 5 grams of 9-bromophenanthrene (m.p. 63-64°) was added in a current of nitrogen to a freshly prepared and filtered solution of butyllithium (made from 3 g of n-butyl chloride, 0.5 g of lithium, and 30 ml of absolute ether). The 9-phenanthryllithium settled out as a white crystalline precipitate that was insoluble in ether. The phenanthryllithium was allowed to settle for a few minutes, and then the ether layer was decanted and the organolithium compound twice extracted with ether (30 ml) and decanted. The washed 9-phenanthryllithium was suspended in 40 ml of ether, and 0.9 g of phosphorus trichloride diluted with 20 ml of absolute ether was added, with constant agitation, during the course of 15-20 minutes. Considerable heat was evolved, and the reaction mass first turned pink and then red. After half the phosphorus trichloride had been added, a precipitate began to settle out, and the color slowly disappeared. The reaction mass was decomposed with water, and the resultant precipitate was filtered out. This yielded 3.32 g of a substance with an m.p. of 358-365°. Double recrystallization from toluene yielded 2.6 g of tri-(9-phenanthryl)-phosphine as colorless lamellae with an m.p. of 374-376°. The yield was 72% of the theoretical, based on the 9-bromophenanthrene used for the reaction.

0.1177 g substance: 0.3638 g $(NH_4)_3PO_4 \cdot 12\,MoO_3$. Found %: P 5.12. $C_{42}H_{27}P$. Calculated %: P 5.53.

Tri-(9-anthryl)-phosphine. 5 grams of 9-bromoanthracene (m.p. 98-100°) was added to a freshly prepared and filtered solution of butyllithium (made from 3 g of n-butyl chloride, 0.5 g of lithium, and 30 ml of absolute ether). 0.9 g of phosphorus trichloride, diluted with 25 ml of absolute ether, was gradually added, with agitation and chilling with ice, to the resultant 9-anthryllithium, which had settled out as a yellow precipitate. During the course of the reaction the color of the reaction mass changed from green to brown-red. The reaction mass was decomposed with water, the ether solution washed with a little water, and half of the ether driven off. The precipitated orange-red crystalline deposit was filtered out (1.25 g; m.p. 160-240°), while the mother liquor was evaporated to a total volume of 10-12 ml. This precipitated 0.5 g of a substance with an m.p. of 160-205°. The product with an m.p. of 160-240° was twice recrystallized from benzene, yielding 0.84 g of tri-(9-anthryl)-phosphine as orange-red lamellae with an m.p. of 270-273° (20% yield).

0.0464 g substance: 0.1553 g $(NH_4)_3PO_4 \cdot 12MoO_3$. Found %: P 5.71. $C_{42}H_{27}P$. Calculated %: P 5.51.

The benzene mother liquors yielded 0.25 g of anthracene (m.p. 214-216°).

Crystallizing the fraction with a m.p. of 160-205° from benzene yielded another 0.4 g of anthracene (m.p. 213-215°). The anthracene totaled 18% of the theoretically possible.

Tri-(9-bromoanthryl-10)-phosphine. 5 g (0.014 mole) of 9,10-dibromoanthracene (m.p. 220-222°) was added to 32 ml of an ether solution of phenyllithium (0.017 mole). Twenty minutes later, an ether solution (15 ml) of 0.67 g of phosphorus trichloride was added to the ice-chilled and stirred solution. The addition of the first few drops turned the reaction mass red. A red precipitate was thrown down, its total increasing as the chloride was added. Ten minutes after the reagents had been mixed, the reaction mass was decomposed with water, and the crystalline precipitate (3.1 g; m.p. 160-200°) was filtered out. The latter was boiled with 250 ml of toluene, the solution then being filtered and cooled. As the solution stood, 1.2 g of tri-(9-bromoanthryl-10)-phosphine as lustrous orange-yellow lamellae with a m.p. of 205-208° settled out.

0.1645 g substance: 0.3524 g $(NH_4)_3PO_4 \cdot 12MoO_3$. Found %: P 3.48. $C_{42}H_{24}Br_3P$. Calculated %: P 3.88.

Tri-(1,2-benzanthryl)-phosphine. 2 g of 10-bromo-1,2-benzanthracene was added to a solution of n-butyllithium, prepared from 1.1 g of n-butyl chloride, 0.2 g of finely cut lithium, and 20 ml of absolute ether. An ether solution of 0.35 g of phosphorus trichloride was chilled and then gradually added to the resultant 1,2-benzanthryl-10-lithium [8]. The reaction, which involved the liberation of heat, was accompanied by the solution's turning orange-yellow and by the precipitation, toward the end of the reaction, of an abundant light-yellow, amorphous precipitate. After the reaction mass had been treated with water, the finely crystalline precipitate (0.52 g) was filtered out, and the ether solution was concentrated to small volume. This yielded another 0.3 g of the substance as minute lamellae with a m.p. of 190-193°.

The synthesized substance was very sparingly soluble in organic solvents. The substance was treated with boiling benzene before being analyzed. M.p. 192-194°. The yield totaled 53%.

0.0822 g substance: 0.2247 g $(NH_4)_3PO_4 \cdot 12MoO_3$. Found %: P 4.49. $C_{54}H_{33}P$. Calculated %: P 4.35.

Triphenylphosphine oxide. A solution of phenyllithium (made from 5 g of bromobenzene, 0.44 g of lithium, and 30 ml of ether) was chilled with ice, and 1.6 g of phosphorus oxychloride, diluted with 20 ml of absolute ether, was added. The reaction is extremely violent, the solution turning a brown-black. Ten minutes later the reaction mass was poured into water. The amorphous precipitate that settled out at first gradually decomposed, and the reaction product was converted into an ether solution. The latter was treated with water, the ether was driven off until its volume was 1/4 of the original volume, and the precipitated substance was filtered out. This yielded 1.6 g of a substance with a m.p. of 152-154°. Another 0.45 g of a substance with a m.p. of 151-153° was recovered from the concentrated mother liquor. Crystallization from ether of both fractions yielded 1.7 g of triphenylphosphine with a m.p. of 155-157°. The yield totaled 65%, based on bromobenzene.

Tri-(α-naphthyl)-phosphine oxide. An ether solution of α-naphthyllithium, prepared from 8 g of α-bromonaphthalene, 0.54 g of lithium, and 45 ml of absolute ether, was chilled with ice and agitated while 1.6 g of phosphorus oxychloride in 20 ml of absolute ether was added. During the reaction the color changed from brown to coffee color, and an abundant precipitate settled out. The reaction mass was allowed to stand for half an hour at room temperature and then decomposed with water. The crystalline precipitate was filtered out (1.9 g, m.p. 305-312°), and the ether solution was washed with water and concentrated to 1/4 of its original volume. This yielded another 0.7 g of a substance with a m.p. of 296-305°. Double recrystallization from a large quantity of chloroform yielded 2.1 g (38.5%) of tri-(α-naphthyl)-phosphine, with a m.p. of 335-336.5°.

4.560 mg substance: 13.967 mg CO_2; 2.095 mg H_2O. Found %: C 83.59; H 5.14. $C_{30}H_{21}OP$.
Calculated %: C 84.07; H 4.91.

Tri-(9-phenanthryl)-phosphine. 30 ml of absolute ether was added to freshly prepared 9-phenanthryllithium, prepared from 5 g of bromophenanthrene by the procedure described above and washed with ether, after which it was chilled and stirred while 0.9 g of phosphorus oxychloride diluted with 30 ml of ether was added. Considerable heat was liberated, and an amorphous white precipitate was thrown down. The reaction mass was set aside for 10 minutes and then decomposed with water. The colorless crystalline precipitate that formed at the boundary between the two layers was filtered out (3.1 g; m.p. 295-315°). Double recrystallization of the precipitate from toluene yielded 1.8 g of a colorless finely crystalline substance with a m.p. of 354-356°. The yield of the tri-(9-phenanthryl)-phosphine oxide was 49%, based on the 9-bromophenanthrene used for the reaction.

0.1934 g substance: 0.5960 g $(NH_4)_3PO_4 \cdot 12MoO_3$. Found %: P 5.27. $C_{42}H_{27}PO$. Calc.%: P.536.

Tri-(1,2-benzanthryl)-phosphine oxide. 0.5 g of phosphorus oxychloride, diluted with 40 ml of ether, was slowly added, with chilling, to 1,2-benzanthryl-10-lithium, prepared from 3 g of 10-bromo-1,2-benzanthracene and n-butyllithium [8]. As the reagent was added, the organolithium compound disappeared and an amorphous light-yellow precipitate settled out. After the reaction mass had been treated with water, the yellow precipitate floating between the ether and aqueous layers was filtered out and dried. This yielded 1.5 g of tri-(1,2-benzanthryl)-phosphine oxide, with a m.p. of 184-187°, or 63% of the theoretical. The substance was refined by crystallizing it from a benzene-ether mixture. It consisted of extremely minute light-yellow lamellae with a m.p. of 191-193°.

0.1188 g substance: 0.3102 g $(NH_4)_3PO_4 \cdot 12MoO_3$. Found %: P 4.36. $C_{54}H_{33}PO$. Calculated %: P 4.26.

SUMMARY

Organolithium reagents can be used in synthesizing carbocyclic compounds of phosphorus. Triaryl phosphines are synthesized by reacting phosphorus trichloride with aryl lithium compounds, while triaryl phosphine oxides are produced by reacting phosphorus oxychloride with aryl lithium compounds. This method makes it possible to synthesize the simplest compounds of this type, as well as phosphinic derivatives of tricyclic and tetracyclic hydrocarbons.

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Received August 28, 1950.

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NEW TYPES OF TERPENE TRANSFORMATIONS

VI. THE ACTION OF CHLORINE UPON α-TERPINENE

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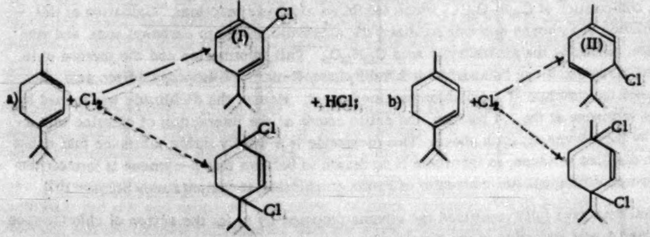
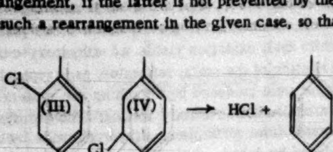
In previous reports [1] we have described the action of chlorine upon α- and β-pinenes, dipentene, terpinolene, and Δ³-carene. In all these cases, the principal reaction products proved to be unsaturated monochlorides with a shifted double bond, in conformity with the theoretical consideration we have developed. These initial terpenes have no conjugated double bonds; α-terpinene has such double bonds, but branched at the ends. In the light of the generally accepted notions of the interaction of conjugated dienes with halogens, we might have supposed that the action of chlorine upon α-terpinene would result in the addition of chlorine at the 1,4 position, yielding 1,4-dichloroparamenthene-2. There is no reason to think that addition will occur, in contrast to the Thiele rule, at the 1,2 and 3,4 positions, since the α-terpinene molecule has no sharply polar substituents. At the start of this research we had reason to believe, however, that the reaction can follow another course, as will be set forth later, viz.: the same "anomalous" M.D.Lvov reaction as exists for the terpenes mentioned above.

Both the double bonds of α-terpinene are equally branched, in contrast to the bonds in dipentene and terpinolene, so that two possibilities must be considered when we discuss the possible mechanism of the reaction:



Will these monochlorides be stable? We already know [1] that the monochlorides of terpinolene and carene are decomposed by heating above 50-60°, giving off hydrogen chloride. Morever, we know that the terpene monochlorides undergo an allyl rearrangement, if the latter is not prevented by the Bredt and semicyclic exclusion principles. There is no obstacle to such a rearrangement in the given case, so that we ought to obtain the chlorides (III) and (IV), respectively:



The two monochlorides (III) and (IV) are derivatives of dihydrobenzene and ought to be more readily decomposed, with the evolution of hydrogen chloride, than the monochlorides of terpinolene and carene, since this reaction results in the formation of p-cymene, an aromatic hydrocarbon, corresponding to a transition from dihydrobenzene to benzene. The latter transformation is accompanied by the liberation of energy, totaling some 20 cal per mole [2] ("ring aromatization energy").

If the supposed formation of p-cymene is borne out by experiment, it will constitute a new exception to the Thiele rule. Up to now the sole exception to this rule has been 1,2 addition. Our instance is an exception of no little theoretical significance. Its discovery compels us to re-examine the so-called resonance theory, even if this be supererogatory.

Even external observation of the reaction of chlorine with α-terpinene shows that this reaction differs from that involving the other terpenes mentioned above. The temperature of the reaction medium is kept within the -5 to $-8°$ range, except for α-terpinene, when ice and snow are used for chilling, when the chlorine pass-through rate is the same, ., and when equal volumes of terpenes are treated in the same apparatus. In the case of α-terpinene the temperature rises rapidly to $+15$ and $+25°$; hence, the chlorine must be fed in at a much lower rate of flow in order to avoid overheating and to keep the temperature within the same boundaries of -5 to $-8°$. With all the terpenes the volumetric rate at which carbon dioxide is evolved is lower than the chlorine rate of supply, though it is higher in the case of α-terpinene. The percentage of the "anomalous" reaction did not exceed 90% for all the terpenes, while it fluctuated about 125% in the case of α-terpinene. This paradoxical figure is explained below.

After a few preliminary tests, we ran a pilot-plant experiment, using all precautions to ensure obtaining a true picture of the reaction (see the experimental section). Analysis of the reaction products fully confirmed the considerations set forth above. No monochloride was found; instead of it we found p-cymene, its yield being proportional to the "anomalous" reaction ($\frac{125}{2} = 63\%$). The residue consisted almost entirely of the dichloride. The dichloride yield approximated the calculated value ($\sim 37\%$). It should be noted that no hydrogen chloride was evolved during fractionation of the reaction products, as in the fractionation of the products of the chlorination of carene and terpinolene at high temperatures. Hence, at temperatures below $-10°$, the monochlorides (I) or (II) [(III) or (IV)] are decomposed at the instant they are produced in the reaction medium, two molecules of hydrogen chloride being evolved per molecule of p-cymene, thus explaining the h yield of the "anomalous" reaction (127%) which is absurd at first glance. As a matter of fact, the yield is half the figure given above.

The structure of the dichloride was established by ozonation followed by oxidation. Ozonating the dichloride with an excess of ozone and decomposing the ozonide with cold water in the presence of platinum black yielded a substance with the composition of $C_{10}H_{16}O_2Cl_2$, which exhibited aldehyde reactions. Oxidation of this substance with an alkaline solution of hydrogen peroxide oxidized the aldehydic groups to carboxyl ones, and saponified the two chlorine atoms, producing the dicarboxylic acid $C_{10}H_{18}O_6$. This information and the method of its synthesis indicate that the only structure it can be assigned is 2,5-dihydroxy-2-methyl-5-isopropyladipic acid, the initial dichloride being assigned the structure of 1,4-dichloroparamethene-2. Hence, the dichloride was formed by the addition of chlorine to α-terpinene at the 1,4 position, the entire course of the interaction of chlorine with α-terpinene being represented by the schema set forth above. This dichloride is a wholly stable substance that suffers no change in storage or when distilled in vacuo, so that there is no reason to believe that p-cymene is formed from the dichloride in our instance by splitting out two molecules of hydrogen chloride at temperatures below $-10°$.

Thus, our experimental data have fully confirmed the schema proposed by us for the action of chlorine upon α-terpinene and have discovered a new exception to the Thiele rule.

In conclusion, let us dwell upon the problem of the production of pure α-terpinene. When we turn to the pertinent literature [3], we find that different authors cite highly divergent constants for this terpene: b.p. from 170 to 181°; the d_4^{20} from 0.837 to 0.845 and even 0.855 (!) [4]. At the same time it may be noted that the same figures indicate that the samples of α-terpinene with a specific gravity below 0.842 produce a satisfactory yield of the characteristic nitrosite of α-terpinene, while their oxidation yields $\alpha\delta$-dihydroxy-α-methyl-δ-isopropyladipic acid; they also exhibit a rather appreciable exaltation of the molar refraction, as is typical of a substance with conjugated double bonds. These samples of α-terpinene were produced by detaching two molecules of hydrogen chloride from α-terpinene dihydrochloride by the action of alkalies or tertiary amines. The samples of α-terpinene produced by detaching two molecules of hydrogen chloride from α-terpinene dihydrochloride by the action of alkalies or tertiary amines. The samples of α-terpinene produced by dehydrating terpineol have a high specific gravity and do not produce high yields of the nitrosite or the above-named acid.

It was natural to suppose that dehydration of terpineol would yield, in addition to α-terpineol and terpinolene, 1,8-cineole, with a sp.gr. of 0.930 and a b.p. of 174.5°, which does not react with sodium. To check these inaccuracies we prepared 1.5 kg of the terpineol dehydration product and fractionated it at 11 mm pressure into a column with an efficiency of about 20 theoretical trays and a reflux ratio of 12-15. The fractions with a b.p. of 55-58° furnished a good yield of the nitrosite and an oily, decomposable polybromide (characteristic of α-terpinene); the high-boiling fractions yielded no nitrosite, but did yield a crystalline tetrabromide that is characteristic of terpinolene. The α-terpinene fractions boiled at from 172.5° to 174.5° at atmospheric pressure and had a sp.gr. of 0.848 to 0.845, i.e., was clearly unusable. Analysis showed that these fractions contained 3.5 to 4% of oxygen, i.e., about 30% of cineole. We know that cineole constitutes a molecular compound with resorcinol [5] with the composition of $(C_{10}H_{18}O_2)_2 \cdot C_6H_6O_2$ and a m.p. of 80-85°, and, hence, stable below that temperature. Treating these fractions twice with an excess of resorcinol and driving off the α-terpinene *in vacuo* from the cineole complex, followed by rectification into a column, yielded a sample of α-terpinene with the following constants: b.p. 31.5° at 1 mm and 172.5-173.5° at 760 mm; d_4^{20} 0.8398; n_D^{20} 1.4770; MR_D 45.80; calculated 45.24; ΣMR_D 0.56. The constants cited for the purest α-terpinene (as given by the MR_D and the specific gravity) are [6]: b.p. 173.5-174.8°; d_4^{20} 0.8375; n_D^{20} 1.477; MR_D 45.88; ΣMR_D 0.64.

EXPERIMENTAL

The α-terpinene was chlorinated in the manner described [1]. 310 g of α-terpinene, 192 g of $NaHCO_3$, and 70.5 g of chlorine were used. As a result of chilling with snow and salt and of reducing the chlorine rate of flow, the temperature within the reaction mixture did not exceed −10°. The reaction product totaled 325 g, including 25.85 g of chlorine and 45.68 g of chlorine in the form of salts; percentage of anomalous reaction = 126.7.

The excess terpinene was driven off at 0.5 mm with a small packing and a bath temperature that did not exceed 35° (the collector being chilled with snow and salt), the residue totaling 74 g. It was first fractionated molecularly (bath temperature not over 40°). The distillate totaled 57 g, the residue 12 g, and the losses 5 g. The distillate was fractionated into a herringbone column with 2 cm clearance (to avoid loss of vacuum in the flask due to dynamic resistances in the column) at a pressure of $1 \cdot 10^{-3}$ mm. This yielded 12.5 g of a fraction up to 27° (principally 24-27°), 32 g of a 27-31° fraction, plus a residue of 2.5 g and a loss of 10.0 g (bath temperature not above 40°).

For the 27-31° fraction: d_4^{20} 1.007; n_D^{20} 1.4966. Found % Cl 33.4. $C_{10}H_{16}Cl_2$. Calculated %: Cl 34.6.

Analysis of the hydrocarbon fraction distilled from the chlorination product (242 g). The terpenes were eliminated from 100 ml (85 g) by triple agitation with an equal volume of sulfuric acid (sp.gr. 1.73), which dissolves the terpenes but does not act upon the aromatic hydrocarbons. The first agitation evolved considerable heat, less being evolved in the second agitation, and none in the third. The oily layer was driven off with steam, and the hydrocarbon dried and distilled. It all boiled at 175-176° (33 g); its constants were: d_4^{20} 0.855; d_4^{15} 0.8606; n_D^{15} 1.4922. Oxidizing the hydrocarbon yielded p-hydroxypropylbenzoic acid, with the constants that are typical of that acid; hence, the hydrocarbon was p-cymene. It totaled 86.8 g. If we take the high-boiling residue to be a dichloride, which is quite close to actuality, its yield was 74 g. The possible yields were: monochloride $136 \cdot 0.69 \cdot \frac{170}{136} = 107$ g, of which $136 \cdot 0.63 \cdot \frac{134}{136} = 84.4$ g of cymene; $136 \cdot 0.37 \frac{207}{136} = 76.6$ g of the dichloride, where 136 is the weight of the terpinene reacting with 1 g of chlorine; $0.63 = 63\% = \frac{126}{2}$ = the theoretical yield of the monochloride; 0.37 = the theoretical yield of the dichloride; 136, 170, 207, and 134 are the respective molecular weights of terpinene, the monochloride, the dichloride, and cymene.

Investigation of the structure of the dichloride. *Ozonation.* 5 g of the dichloride in chloroform was chilled with snow and salt and saturated with ozone (44 liters, containing 5% of ozone). The chloroform was driven off in vacuum, and the ozonide decomposed with ice water containing platinum black until its reaction for a peroxide was negative. The water-insoluble substance weighed 6.0 g and exhibited aldehyde reactions.

Found %: Cl 26.6, 26.1; C 48.0, 47.8; H 7.1, 7.0. $C_{10}H_{16}O_2Cl_2$. Calc.%: Cl 29.7; C 50.2; H 6.7.

2.7 g was stirred with an excess of an alkaline solution of hydrogen peroxide until it dissolved. The solution was acidulated and extracted with ether, and the ether was driven off. The residue crystallized and contained no chlorine.

Found %: C 51.4, 51.5; H 7.8, 7.8. $C_{10}H_{18}O_6$. Calculated %: C 51.3; H 7.7.

The acid was decomposed by treating it with lead peroxide, carbon dioxide being liberated; hence, it was an α-hydroxy acid. The silver salt of the acid was prepared in the usual manner.

Found %: Ag 47.9. $C_{10}H_{16}O_6Ag_2$. Calculated %: Ag 48.2

Synthesis of α-terpinene. 1800 g of terpineol was added a drop at a time to a boiling saturated solution of oxalic acid. The distillate contained 1556 g of oil. The latter was distilled from a Würtz flask at 2 mm, the 37-48° fraction totaling 1462 g.

This fraction was fractionated at 11 mm into a column with an efficiency of 20 theoretical trays and a reflux ratio of 8. After three fractionations we secured (see table):

Fraction No.	B.p.	Wt. (g)	B.p. at 760 mm	d_4^{20}	Production of nitrosite	Bromination
I	51–56°	39	Up to 173°	0.851	—	Liquid, decomposes
II	56	203	172.5–174	0.848	M.p.154°	"
III	56–57.5	152	173.5–174.5	0.846		
IV	57.5–60	82	174–176	0.845	Little	
V	60–65	–	–	–	None	Crystals
VI	65–68	–	–	–	None	

Fractions II, III, and IV were combined and heated on a water bath with 20% of their aggregate weight of resorcinol, with stirring. Within two hours the resorcinol deliquesced into a heavy oil, after which the α-terpinene was driven off at 1 mm from the coordination compound, and the above procedure was repeated (not all the resorcinol deliquesced). The α-terpinene driven off was fractionated at 1 mm in the column mentioned above, a fraction with a b.p. of 31.5° being collected (325 g). The high-boiling fractions yielded pure terpinolene, as reported earlier [1]

SUMMARY

1. The action of chlorine upon α-terpinene has been investigated for the first time.

2. It has been shown that, in conformity with the theoretical considerations we have advanced, the principal reaction product is p-cymene, produced by the by-product 1,4-dichloro-p-menthene-2 splitting hydrogen chloride out of the chloride (I) or (II) after the latter had undergone an allyl rearrangement to the chloride (III) or (IV).

3. This demonstrates that the Thiele rule does not apply to this case, which constitutes a new type of the rule's inapplicability.

4. A method is set forth for securing pure α-terpinene from terpineol.

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Received September 13, 1950

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NEW TYPES OF TERPENE TRANSFORMATIONS

VII. THE SYNTHESIS OF ALCOHOLS AND ETHERS FROM CHLOROTERPENES

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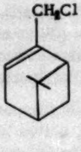
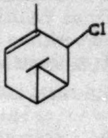
In our preceding reports [1] we have described the synthesis of chloroterpenes, produced by reacting the terpenes with chlorine. These chlorides are terpene derivatives with the same degree of saturation and the same carbon skeleton as the original terpene, but with a shifted double bond, chlorides of the allylic type. In these papers we also have indicated the temperature range within which these chlorides are stable, set forth the possibility or impossibility of their allyl rearrangement (Bredt and semicyclic exclusion principles), and demonstrated that these latter conclusions are borne out by experiment. In our first report we noted that these allylic chloroterpenes may serve as the initial substances for the synthesis of various terpene derivatives possessing the same carbon skeleton and the same degree of unsaturation as the original terpene, their common formula being $C_{10}H_{15}X$, where X is any atom or group of atoms. Derivatives of this kind are either wholly unknown or else accessible only with difficulty at the present time. The present report sets forth some general considerations governing the anion exchange reactions of allylic chlorides and reports the results of our research on the synthesis of the respective alcohols and ethers, with the general formula of $C_{10}H_{15}X$, from 7-chloro-α-pinene (I), 3-chloro-Δ^4-carene (II), 4-chlorodipentene (III), and chloroisosantene (IV).


(I)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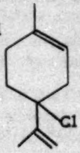
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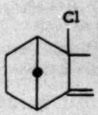
(IV)

We have previously set forth considerations, which have been confirmed experimentally, to the effect that these chlorides must not undergo an allyl rearrangement when heated. These same considerations enable us to assert that no allyl rearrangement will occur when a chlorine atom is exchanged for any radical [the semicyclic exclusion principle in the chlorides (I) and (III); the elimination of the double bond conjugated to the three-membered ring in the chloride (II); and the greater strain existent in the structure of santene than in isosantene in the chloride (IV)]. As we shall see below, this prediction is borne out by experiment.

The conversion of allylic chlorides to any other derivatives in anion exchange reactions requires that we know the order of these reactions if we are to control them consciously. In 1939 one of the authors of the present paper found that the saponification of allyl chloride is a unimolecular reaction. The same was found to be the case with as-dichloromethylethylene [2]. This may serve as a basis for our supposing that the anion exchange reactions of all allylic chlorides, including our chloroterpenes, are unimolecular. The velocity that governs the rate of overall transformation will be the rate of dissociation of the allylic chloride into the chlorine anion and the organic cation. Then the latter will coordinate with another anion or with the anions present in the reaction medium; therefore, if our aim is a maximum yield of a given compound, we must see to it that the reaction medium contains no anions but the one whose derivative is the given compound. For example, as we shall demonstrate below, chloroterpenes must not be reacted with potassium acetate in an alcoholic solution, as we would get an appreciable percentage of an ether, in addition to the desired ester, notwithstanding the negligible concentration of the alkoxyl ion in the solution. Moreover these facts indirectly confirm the unimolecularity of the anion exchange reaction of our chloroterpenes.

The following relationship was established long ago for the velocities of the anion exchange reactions of saturated chlorides: tertiary ≫ secondary > primary. The same holds true for the chloroterpenes, which are chlorides of an allylic type. In exchange reactions with potassium acetate the chloride (I) (primary) requires heating for four hours in an acetic acid solution (117°) if the reaction is to be complete; the chloride (II) requires only two hours of heating, and the chlorides (III) and (IV) require only 20 minutes of heating at 50°, which is equivalent to approximately 10 seconds at 117°.

The direct saponification of the chloroterpenes (especially the primary and secondary ones) is not a convenient method of synthesizing the respective alcohols from them. The reaction drags out for dozens of hours, apparently because of the negligible solubility of the chloroterpenes in boiling water or in solutions of alkali carbonates, resulting in considerable tarring of the reaction products, and still the reaction remains incomplete. Inasmuch as the boiling points of the chloroterpenes lie in approximately the same range as those of the respective alcohols, they cannot be separated thoroughly by fractionation. We also get high-boiling products, evidently diterpenyl ethers. We therefore abandoned direct saponification and tried roundabout saponification, via the esters. This method yielded fully satisfactory results.

Putting this method into practice is not difficult: the chloroterpene is heated for some time to some temperature or other with a solution of anhydrous potassium acetate in anhydrous acetic acid. The precipitated potassium chloride, which is slightly soluble in the reaction medium, enables one to check the progress of the reaction: if the potassium chloride is suction-filtered out and the filtrate reheated, the absence of any newly formed precipitate indicates that the reaction is complete.

In the case of the chloride (I), the reaction follows a single path, producing only the acetate of myrtenol (7-hydroxy-α-pinene) boiling in an interval of one or two degrees. This chloride remains stable even at relatively high temperatures. The chlorides (II) and (III), which decomposed when heated yield $C_{10}H_{14}$ hydrocarbons as the result of the splitting out of hydrogen chloride, in addition to the corresponding esters. Though the chloride (IV) is stable when heated, it behaves in the same way, the yield of the hydrocarbon being smaller. We produced these hydrocarbons, "dehydroterpenes," from the same and from other chloroterpenes, as well as by different methods. They have the same composition as cymene, but are not aromatic hydrocarbons. Their properties are quite unusual.

In every case we secured acetates of the alcohols that are not products of an anion exchange involving an allyl rearrangement that occurs at the instant of exchange, the chloride (I) yielding an ester of pyrtenol, the chloride (II) an ester of 3-hydroxy-Δ^4-carene, the chloride (III) an ester of 4-hydroxydipentene, and the chloride (IV) an ester of tertiary isosantenol; in other words, the chlorine in these chlorides is replaced by an acetic acid residue with any rearrangement taking place, in agreement with the theoretical considerations referred to above.

The esters (I) and (III) ($OCOCH_3$ instead of Cl) smell like cedar oil (Juniperus virginiana); the ester (II) has the persistent and strong odor of eau de cologne, and the ester (IV) smells like camphor. The reaction product yields are below those expected, owing to their volatility with the solvent, acetic acid. If so desired, they may be extracted from the latter with light gasoline, after dilution with water. It is simpler and more satisfactory to repeat the operation on the driven-off acetic acid. The acetates are saponified by heating them with an alcoholic solution of an alkali. The yields of alcohols, based on the esters, are nearly quantitative.

It should be noted that the alcohols produced are apparently of very high purity. It has been said, for example, that the phenylurethane of myrtenol (isolated from the essential oil of myrtle) cannot be secured in crystalline form [3], though we have secured it in crystals; 114-115° is given as the melting point of myrtenyl acid phthalate [3], whereas the ester of our synthetic myrtenol has a m.p. of 117-118°. The phenylurethane of carenol (II) also crystallized within 24 hours after its synthesis. Anyone who has worked with terpene derivatives knows how hard it is to secure them in the crystalline state whenever they are not pure enough.

Myrtenol [(I), with OH replacing Cl] is known, but the alcohols (II), (III), and (IV) have been synthesized for the first time, which is true of their esters as well. Their synthesis, like that of carveol (see Report III), opens the way to various syntheses in the terpene and homoterpene series, based on the chloroterpenes synthesized for the first time.

It should be possible to synthesize ethers of terpene alcohols by reacting a sodium alcoholate dissolved in the respective alcohol upon the chloroterpenes. We have found that these ethers are secured with a fairly high yield by reacting chloroterpenes with an alcoholic solution of an alkali. This method was checked for the chloride (I): we secured the methyl, ethyl, and isoamyl ethers, hitherto unknown liquids with peculiar, unpleasant odors.

EXPERIMENTAL

Synthesis of myrtenol. (by D. Tishchenko). The chloride (I) had a b.p. of 85.5-87° at 11 mm; d_4^{20} 1.0065; n_D^{20} 1.4976; $[\alpha]_D^{16}$ (10 cm) = + 21.8°; its total chlorine was 19.9%, its active chlorine was 19.8%. Direct saponification: 50 g of the chloride, 15 g of chalk, 200 ml of water. The mixture was stirred in a flask fitted with a reflux condenser on a boiling water bath until no more carbon dioxide was evolved (26 hours). The undissolved chalk totaled 4.2 g, the reaction being 74% complete. The 47 g of oil was separated and fractionated. It distilled below 120°, the first runnings containing chlorine, the middle fractions containing 8-9% of hydroxyl ($C_{10}H_{16}O$ contains 11.2% OH), the end fractions containing no hydroxyl. This method was discarded in view of its obvious unsuitability.

Synthesis of myrtenyl acetate. 1. Action of potassium acetate in methanol. 100 g of the chloride, 65 g of the fused salt (60 g called for theoretically), 300 ml of methanol. 36.6 g of KCl was precipitated after 8 hours of refluxing, with another 2.2 g settling out after another 8 hours. The solution was diluted with fourfold its volume of water and then extracted with ether. The aqueous solution was found to contain 2.3 g of KCl, making a total of 41.1 g; the possible total was 42.0 g. The ether was driven out of the ether layer, and the residue fractionated at 10 mm into a column with an efficiency of 4-5 theoretical trays. This yielded: Fraction I 81-83° – 29.0 g; Fraction II 83-110° – 12.6 g; Fraction III 110-112° – 51.2 g; and a residue of 5.2 g. Fraction I contained traces of chlorine.

Fraction I: d_4^{18} 0.937; n_D^{18} 1.4832.

Found %: C 78.7, 78.9; H 10.8, 10.8; OCH_3 16.5, 16.2. $C_{10}H_{15}OCH_3$. Calculated %: C 79.5; H 10.8; OCH_3 18.8.

Fraction III: d_4^{20} 0.989; n_D^{20} 1.4743; $[\alpha]_D^{14}$ (10 cm) = + 29.3°.

Found %: C 74.0, 74.1; H 9.4, 9.5; saponification value 282, 284. $C_{12}H_{18}O_2$.
Calculated %: C 74.2; H 9.3; saponification value 288.

The yield of the ether (Fraction II divided in half) was 37% of the theoretical, that of the ester being 51%.

2. The same in ethyl alcohol. See above for the quantities of reagents used and the experimental conditions. The methanol was replaced by ethyl alcohol. The reaction was 92% complete after 12 hours of boiling. We secured about 25% of the theoretical yield of ethyl myrtenyl ether [d_4^{20} 0.925; n_D^{20} 1.4728; $[\alpha]_D^{14}$ (10 cm) = + 10.7°; % OC_2H_5 21.8 and 21.6], and about 60% of myrtenyl acetate (d_4^{20} 0.990; n_D^{20} 1.4834; saponification value 286 and 287).

3. The same in acetic acid. 100 g of the chloride (I), 65 g of the fused salt, and 300 ml of acetic acid. The reaction was completed after 3.5 hours of refluxing. 39.8 g of KCl was found in the precipitate and the solution. The acetic acid was driven off in a water-jet vacuum with a herringbone packing, the residue being distilled with steam, and the oil being separated and fractionated at 20 mm into a column with an efficiency of 4-5 theoretical trays.

This yielded: 6.5 g of a fraction up to 120°; 82.3 g of a 120-122° fraction, and 5.0 g of residue. The fraction was myrtenyl acetate, as indicated by its constants (d_4^{20} 0.9905; n_D^{20} 1.4744, saponification value 286 and 286) and by its yielding myrtenol upon saponification (vide infra). The acetate yield was not below 72%. The principal losses were in the acetic acid driven off; when this acid was diluted with water, it grew turbid, an oily layer with the odor of myrtenyl acetate floating on top.

Saponification of myrtenyl acetate. 223 g of the acetate was refluxed in a flask on a boiling bath together with 75 g of potassium hydroxide and 400 ml of alcohol. The alcohol was driven off into a herringbone column, the residue diluted with water to make 1 liter and then extracted with ether, the ether being driven off and the residue fractionated at 13 mm into a column with an efficiency of 4-5 theoretical trays. This yielded: 5.0 g of a fraction up to 106.5°; 163.5 g of a 106.5-107° fraction; and 4.0 g of residue. The alcohol yield was at least 94%.

106.5-107° fraction: d_4^{26} 0.9746; n_D^{26} 1.4960; $[\alpha]_D^{26}$ (10 cm) = + 29.1°.

Found: MR_D 45.55. $C_{10}H_{15}OH\,\mathsf{F}_{\square}$. Calculated 45.43. Found %: C 78.6. 78.5; H 10.6, 10.4. $C_{10}H_{16}O$.
Calculated %: C 78.8; H 10.5.

Myrtenyl acid phthalate. 5 g of phthalic anhydride was heated with 5 g of alcohol to 100° until they dissolved in each other. After the melt had solidified, it was treated with an aqueous soda solution, dissolving completely. The solution was acidulated, and the acid suction-filtered out, dried, and dissolved in chloroform. The undissolved residue totaled 0.15 g. The chloroform was driven off, and the crystals were recrystallized from boiling gasoline (80-100°). The m.p. was 113-115° after the first crystallization, being raised to 117-118° after the second and third crystallizations. The gram equivalent was found to be 300; the figure for $C_{18}H_{20}O_4$ is 300.

Inasmuch as secondary alcohols react with phthalic anhydride at temperatures above 125°, while tertiary alcohols do not [5], the alcohol must be taken to be a primary one.

Phenylurethane of myrtenol. 1 g of the alcohol was sealed into a tube with 1 g of phenyl isocyanate and heated to 100° for 1 hour. As the melt cooled, it hardened into a hyaline mass. The mass was dissolved in 50 ml of gasoline (100-110°), and the solution was poured into a beaker. Practically all the contents crystallized within a month, after nearly all the gasoline had evaporated. The crystals were pressed out on paper and recrystallized from gasoline (30-50°) to a constant m.p. of 66-67° (clusters of thin prisms). Subsequent preparations crystallized as soon as a seed crystal was added.

Found %: N 5.3, 5.4. $C_{17}H_{21}O_2N$. Calculated %: N 5.1.

The structure of myrtenol was established by oxidizing it to myrtenal with chromic anhydride in acetic acid, the yield being satisfactory; the myrtenal yielded an oxime with the m.p. of 71-72° that is typical of myrtenaloxime [4]. The oxime was heated with acetic anhydride to convert it into myertenonitrile, which was saponified to myrtenic acid with a m.p. of 52-53° [4] and a gram equivalent of 169 (170 is the calculated value).

Synthesis of carenol (3-hydroxy-Δ^4-carene) (by A.Khovanskaya). Preliminary tests indicated that heating to 117° for 1.5 hours and 2.5-3 hours on a boiling bath would suffice to complete the reaction of the chloride (II) with potassium acetate. The yield of the acetate is low, totaling about 30%; a large percentage of low-boiling fractions of low specific gravity (about 0.9) and high refractive index (about 1.51) plus a viscous, nondistillable residue ("dehydroterpene" and its polymer) being obtained.

We used 20 g of the chloride (II) (%Cl = 17.6), 14 g of fused potassium acetate, and 100 ml of acetic acid, 2.5 hours of heating on a boiling bath. The reaction was more than 92% complete (6.7 g of KCl precipitated, the KCl in the solution being disregarded). The subsequent procedure was the same as that employed for myrtenol. The acetic acid driven off again grew turbid when diluted with water. After the low-boiling fractions (the "dehydroterpene") had been driven off, the acetate fraction was collected: b.p. 91-93° at 4 mm (6.3 g); d_4^{20} 0.987; n_D^{20} 1.4820; MR_D 56.06. $C_{10}H_{15}OCOCH_3 \ulcorner\triangleright$. Calculated: 55.10; ΣMR_D 0.96, indicating the presence of double bonds conjugated with the three-membered ring and the absence of an allyl rearrangement at the instant of the exchange reaction. The experimental saponification value was 282, the calculated value 288. Carenyl acetate is an oily liquid with a very pleasant flowery fragrance.

Saponification of carenyl acetate. 5.1 g of the ester was saponified by boiling it for 4 hours with an excess of alcoholic alkali, after which the alcohol was driven off on a water bath and the residue diluted with three times its weight of water and extracted with gasoline (30-50°). The gasoline was eliminated from the extract, and the residue was fractionated at 5 mm. The principal fraction (4.1 g) boiled at 91°; d_4^{20} 0.969; n_D^{20} 1.5001; MR_D 46.12 $C_{10}H_{15}OH$. Calculated 45.74. The alcohol yield was nearly quantitative. When the experiment was repeated, an alcohol with the following constants: m.p. 80-81° at 0.7 mm; d_4^{20} 0.967; n_D^{20} 1.4987; MR_D 46.12. The alcohol has a strong flowery odor and does not react with phthalic anhydride in boiling benzene; hence, it is not a primary alcohol [5].

Phenylurethane of carenol. 0.85 g of the alcohol was sealed into a test tube together with 0.7 g of phenyl isocyanate and heated on a boiling bath for 6 hours. The contents of the test tube crystallized completely within 24 hours. The contents dissolved completely in gasoline at 100° (no diphenylurea; the alcohol is not a tertiary one). As it cooled, crystals settled out. The m.p. was constant at 121° after a second crystallization.

Synthesis of the alcohols from the monochlorides of terpinolene (III) and santene (IV) (by T.Danilova). Synthesis of dipentenol-4 via its acetic ester. Preliminary tests indicated that the reaction of the chloride (III) with potassium acetate is complete within 20 minutes at 50° or within 24 hours at 15°. Much less of the acetic ester is secured than of the "dehydroterpene" or its polymer.

We used 49 g of the chloride, 50 g of the potassium acetate, and 300 ml of acetic acid. The mixture was allowed to stand at 15° for 24 hours. The 15.3 g of KCl was suction-filtered out, the dissolved KCl being disregarded; the reaction was at least 87% complete. The solution was diluted with water to make 1 liter and then extracted with gasoline (30-50°), the gasoline being driven off and the residue fractionated into a column with an efficiency of 4-5 theoretical trays. This yielded 19.5 g of "dehydroterpene" fractions (d_4^{20} 0.90, n_D^{20} ~1.51), 6.5 g of a fraction with a b.p. of 40-41° at 0.1 mm (d_4^{20} 0.9740; n_D^{20} 1.4923), and 15.0 g of a nondistillable tacky residue (the "dehydroterpene" polymer). The dehydroterpene and its polymer totaled 34.5 g, and the yield of the acetate was 11%.

Saponifying the acetate. 11.2 g of the acetate (40-41° fraction at 0.1 mm in two runs) was heated to boiling for 4 hours with an excess of alcoholic alkali. The alcohol was driven off, and the residue diluted with water; then it was extracted with ether, the ether driven off, and the residue fractionated at 1 mm. This yielded 1.8 g up to 64°, 1.6 g at 64-69°, and 1.3 g at 69-73°.

Fraction constants: d_4^{20} 0.961, 0.967, 0.968; n_D^{20} 1.495, 1.503, 1.508; MR_D 46.22, 46.46, 46.99; % OH 8.3, 9.2, 9.4. $C_{10}H_{15}OH$. F_2. Calculated MR_D 46.77; % OH 11.2. Analysis of Fraction III (69-73°). Found %: C 77.9, 77.9; H 10.8, 10.6. $C_{10}H_{16}O$. Calculated %: C 78.9; H 10.6.

Fraction III did not react with phthalic anhydride in boiling benzene, heating it with phenyl isocyanate yielded diphenylurea, and it was not oxidized by chromic anhydride in acetic acid. Hence, it was a tertiary alcohol, with a structure corresponding to that of chloride (III)(dipentenol-4).

Synthesis of isosantenol. We began by determining that the chloride (IV) reacts nearly completely with potassium acetate in 20 minutes at 50° or in 24 hours at 15°.

We used 23 g of the chloride, 20 g of potassium acetate, and 150 g of acetic acid. The solution was heated to 50° and set aside to stand for 24 hours. The KCl suction-filtered out totaled 9.4 g, the reaction being no less than 86% complete. The filtrate was diluted with water to make half a liter and then extracted with gasoline (30-50°); the gasoline was driven off, leaving a residue of 22 g, which was fractionated into a small column. This yielded: 3.7 g of heads that polymerized in storage ("dehydroterpene", b.p. 30-64° at 7 mm); 14.5 g of fractions representing the acetate (d_4^{20} 1.0;b.p. 60-68° at 2 mm); and 2.6 g of residue. Refraction yielded the principal acetate fraction, with a b.p. of 72-74° at 4 mm; d_4^{20} 1.018; n_D^{20} 1.4773; MR_D 50.03; $C_9H_{13}OCOCH_3$. Calculated 49.78;ΣMR_D + 0.25; the experimental saponification value was 312, the calculated value being 312. The refraction exaltation indicated that a semicyclic double bond was present, as in the chloride (IV) (no allyl rearrangement occurring).

Saponifying isosantenyl acetate. 2 g of the ester was saponified by boiling it for 6 hours with an alcoholic alkali. This yielded an alcohol with a b.p. of 80-86° at 10 mm.

d_4^{20} 1.006; n_D^{20} 1.4972.

Found %: OH 11.5. $C_9H_{13}OH$. Calculated %: OH 12.5

The alcohol did not react with phthalic anhydride in boiling benzene, and smelled like camphor.

Synthesis of ethers of the $C_{10}H_{15}OR$ series. (by D.Tishchenko). The chloride (I) was used in developing this method, which involved heating the chloride with a 20% excess of alkali, dissolved in alcohol, until no more potassium chloride was precipitated. Heating had to be done for 5 hours with methanol, 2¼ hours with ethyl alcohol, and 1 hour with amyl alcohol. The recovery of the ether from the reaction mixture involved driving the alcohol off into a column, diluting the residue with water and extracting it with diethyl ether, driving the diethyl ether off, and fractionating *in vacuo* into a column. The yields of all three ethers were no less than 80%: they were mobile liquids with singular odors and had the following constants:

$C_{10}H_{15}OCH_3$: b.p. 79-81° at 7 mm; d_4^{20} 0.0936; n_D^{20} 1.4836. Found %: OCH_3 17.6, 17.2.

Calculated %: OCH_3 18.8. $C_{10}H_{15}OC_2H_5$; b.p. 94-95° at 15 mm. Found %: OC_2H_5 23.4, 23.0.
Calculated %: OC_2H_5 25.0.

$C_{10}H_{15}OC_5H_{11}$: b.p. 128-130° at 10 mm; d_4^{15} 0.895. Found %: C 81.2, 81.3; H 11.9, 11.7.
Calculated %: C 81.1; H 11.7.

SUMMARY

1. Some points are set forth concerning the anion exchange reactions of the allylic chloroterpenes we have synthesized.

2. It has been shown that saponifying the chloroterpenes with boiling water containing neutralizers is not a suitable method of producing the corresponding alcohols.

3. Reacting potassium acetate with the chloroterpenes in a solution of acetic acid yields acetates of the respective terpenes. The chloroterpenes that are unstable when heated (II and III, and to a lesser degree, IV) also yield "dehydroterpenes", C_nH_{2n-6}, hydrocarbons that are not aromatics.

4. Myrtenol, Δ^4-carenol-3, dipentenol-4, and tertiary isosantenol have been synthesized by saponifying the acetates. The latter three terpenols have been synthesized for the first time.

5. A method is given for synthesizing ethers of $C_{10}H_{15}OR$ terpenols.

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Received September 13, 1950

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THE SYNTHESIS OF CYCLOHEPTANE-1,1-DICARBOXYLIC ACID VIA MALONIC ESTER

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In using the malonic synthesis to synthesize compounds whose molecules contain a four-membered ring, Golmov and Kazansky [1], Kazansky and Lukina [2], and Golmov [3] have shown that this reaction consists of two successive stages: the formation of a γ-halogen alkyl malonic ester by the action of sodium malonic ester upon a 1,3-dihalogen derivative, followed by its cyclization by a sodium alcoholate.

The rather low yield of a cyclic product secured when Kizhner's method [4] is employed is not due to the difficulty of constituting a four-membered ring, as is generally assumed, but to the side reactions that occur during the first stage of the synthesis; the yield of the four-membered ring is some 75% of the theoretical. The overall yield can be increased substantially by choosing conditions that insure a high yield of the intermediate product.

We were also interested in making a similar study of the reaction of sodium malonic ester with other halogen derivatives. This was particularly true of the 1,6-dihalogen derivatives, since we know from the literature [5] that the action of sodium malonic ester upon hexamethylene bromide yields a minute percentage of cyclopentane-1,1-dicarboxylic ester (which has not been isolated in the pure state).

Our previous study of this problem made it seem likely that we could raise the yield of this cyclic product, too, by splitting this reaction into two stages and selecting suitable conditions for each stage. With this in view, we reacted hexamethylene iodide with sodium malonic ester. Our research indicated that this reaction can actually be divided into two phases, with the ζ-iodohexylmalonic ester being initially formed like the γ-bromopropylmalonic ester [3], the yield of the ζ-iodohexylmalonic ester being 33.8% of the theoretical when only the malonic ester is taken in excess. When the reaction involves 4 moles of the malonic ester, 2 moles of the hexamethylene iodide, and 1 gram atom of sodium as an alcoholate, the yield of the ζ-iodohexylmalonic ester totals 51.9% of the theoretical. We were unable to secure a higher yield, since the quantity of hexamethylene iodide at our disposal was too small, but there is no doubt that a higher yield can be obtained by employing a large excess of the hexamethylene iodide. Octane-1,1,8,8-tetracarboxylic ester is formed as a by-product of the reaction.

The second phase of the reaction – the conversion of the ζ-iodohexylmalonic ester into cycloheptane-1,1-dicarboxylic ester by using the customary concentrated solution of sodium alcoholate – furnishes a negligible yield, totaling 3% of the theoretical in our experiments. Thus, the seven-membered ring differs from the four-membered one in being much harder to produce than the latter.

To increase the yield of the cycloheptane-1,1-dicarboxylic ester, we made use of the assertions in the literature that a low reagent concentration was a factor that promoted ring formation.

As we know, this is the principle underlying the Ziegler method of producing compounds with higher ring systems [6]. We therefore reacted the ζ-iodohexylmalonic ester thenceforth with sodium alcoholate in a 0.1-molar solution (an alcohol-benzene mixture), and actually secured cycloheptane-1,1-dicarboxylic ester with a fairly satisfactory yield of 34.7% of the theoretical. Saponifying the cyclopentane-1,1-dicarboxylic ester yielded 93% of the theoretical quantity of cycloheptane-1,1-dicarboxylic acid, which was then converted into cycloheptane carboxylic acid, identical with that described previously [5, 7].

EXPERIMENTAL

The initial substance used in our research was hexamethylene iodide, which we prepared by reacting 1,6-diphenoxyhexane with strong hydriodic acid. 1335 g of trimethylene bromide, freed of propylene bromide by the Gustavson method [8] (b.p. 162-162.5° at 706 mm, d_{21}^{21} 1.9736, n_D^{21} 1.5215, MR_D 31.19, calculated 31.58), yielded 985 g of γ-phenoxybromopropane, with a b.p. of 113-115° at 5 mm.

Reacting an alcoholic solution of the latter with NaI yielded 1084 g of γ-phenoxyiodopropane (b.p. 135-138° at 7 mm), which was then converted into 1,6-diphenoxyhexane by the Würtz method; we made extensive use of the directions contained in the paper by Magidson, Madaeva, and Rubtsov [10]. We secured a total of 220 g of diphenoxyhexane, with a m.p. of 81-83° (from alcohol or benzene).

Diphenoxyhexane is usually converted into hexamethylene iodide by heating it with fuming hydriodic acid in sealed ampoules [11]. It is much simpler, however, to prepare hexamethylene iodide by boiling 1,6-diphenoxyhexane with hydriodidic acid. We refluxed 60 g of diphenoxyhexane with 240 ml of hydriodic acid (sp. gr. 1.76) for 16-20 hours, after which we diluted the liquid with water, separated the lower layer, washed it with alkali and with water, dried it with calcined calcium chloride, and fractionated it in vacuo. This yielded an average of 48 g of a substance that boiled at 135-138° and 6 mm. A crystalline residue was left in the flask. 220 g of diphenoxyhexane yielded 176 g of hexamethylene iodide and 42 g of residue. Reboiling the latter with HI yielded another 39 g of hexamethylene iodide, the total yield being 78.1% of the theoretical.

ζ-Iodohexylmalonic ester. 100 g (0.6 mole) of malonic ester was added to a solution of the alcoholate, prepared from 3.5 g (0.15 gram atom) of sodium and 50 ml of absolute alcohol, after which 100 g (0.3 mole) of hexamethylene iodide was added. After the spontaneous heating had ceased, the reaction mixture was boiled on a bath for 6 hours. After it had cooled, water was added to the flask, the reaction products were extracted with ether, the ether extract was washed with water and a weak hyposulfite solution and dried with calcium chloride, the ether was driven off, and the residue was fractionated in vacuo. This yielded 77.3 g on the average of malonic ester fraction up to 75° at 5 mm, 48 g of hexamethylene iodide (b.p. 125-135° at 3 mm), and 40 g of a fraction with a b.p. of 150-176° at 3 mm. The distillation residue weighed 7.5 g.

Redistillation of the combined 150-176° fractions from three runs yielded 90 g of ζ-iodohexylmalonic ester, which had a b.p. of 169-170° (2.5 mm). The yield was 51.9% of the theoretical.

d_4^{20} 1.3433; n_D^{20} 1.4839; MR_D 78.78; calculated 78.34.

0.2675 g substance: 0.4078 g CO_2; 0.1444 g H_2O. 0.4682 g substance 0.3012 g AgI (by Carius method). Found %: C 41.56; H 6.00; I 34.77. $C_{13}H_{23}O_4I$. Calculated %: C 42.16; H 6.21; I 34.32.

Redistillation in vacuo of the residues of the first distillation yielded the principal fraction, with a b.p. of 226-228° at 7 mm, which was the ester of octane-1,1,8,8-tetracarboxylic acid.

d_4^{20} 1.0591; n_D^{20} 1.4473; MR_D 101.47; calculated 101.18.

0.2552 g substance: 0.5553 g CO_2; 0.1958 g H_2O. Found %: C 59.35; H 8.52. $C_{20}H_{34}O_8$. Calculated %: C 59.70; H 8.45.

This fraction was saponified with an alcoholic KOH solution, the resulting octane-1,1,8,8-tetracarboxylic acid being decarboxylated in a bath at 220-230°, converting it into sebacic acid, with a m.p. of 130-131° after recrystallization from benzene [12]. In other runs, in which no excess of hexamethylene iodide was used, an average of 18.8 g of ζ-iodohexylmalonic ester was secured from 100 g (0.6 mole) of malonic ester, 50 g (0.15 mole) of hexamethylene iodide, and 3.5 g (0.15 gram atom) of metallic sodium. In this case the yield totaled 33.8% of the theoretical.

Cycloheptane-1,1-dicarboxylic ester. 1.3 g of metallic sodium was dissolved in 25 ml of absolute alcohol, 475 ml of anhydrous benzene was added to the alcoholate solution, and then 18.5 g (0.05 mole) of ζ-iodohexylmalonic ester was added. The mixture was refluxed on a water bath for 20 hours, after which as much as possible of the benzene and alcohol was driven off, and water acidulated with sulfuric acid was added to the residue; the resultant oil was extracted with ether, the ether extract was washed with a hyposulfite solution and then with water and dried with calcined calcium chloride, and the ether was driven off, together with the residual benzene, on an oil bath (bath temperature up to 130°). The residue was distilled in vacuo, 5 g of a fraction boiling up to 145 mm at 8 mm being collected. A fairly large amount of a thick, dark oil was left in the flask.

The combined distillates of three runs were redistilled in vacuo with a dephlegmator, yielding 12.6 g of a substance that boiled at 118-121° at 4 mm (8.4 g passed over at 119°). The yield was 34.7% of the theoretical.

d_4^{20} 1.0402; n_D^{20} 1.4558; MR_D 63.21; calculated 63.34.

0.1433 g substance: 0.3377 g CO_2; 0.1654 g H_2O. Found %: C 64.27; H 9.22. $C_{13}H_{22}O_4$. Calculated %: C 64.47; H 9.09.

The substance had a faint fragrance that reminded one of the odor of cyclobutane-1,1-dicarboxylic ester. It behaved like an unsaturated compound when acted upon by a permanganate solution.

Cycloheptane-1,1-dicarboxylic acid. 10.5 g of the ester of cycloheptane-1,1-dicarboxylic acid was saponified for 1.5 hours with a 20% water-alcohol solution of potassium hydroxide, after which the liquid was diluted with water, and the alcohol driven off. After the residue had cooled it was diluted with sulfuric acid, the cycloheptane-1,1-dicarboxylic acid, which was slightly soluble in water, separating as a crystalline precipitate. The latter was suction-filtered, washed with cold water, and dried in a desiccator.

The substance had a m.p. of 177-178° after recrystallization from water. The yield was 7.5 g, or 92.9% of the theoretical.

0.1447 g substance: 0.3085 g CO_2; 0.1016 g H_2O. Found %: C 58.14; H 7.80. $C_9H_{14}O_4$.
Calculated %: C 58.06; H 7.53.

The acid is slightly soluble in cold water, and more soluble in alcohol or ether. Its silver salt is a crystalline precipitate thrown down when a solution of $AgNO_3$ is added to a neutralized solution of the acid.

7 g of dried cycloheptane-1,1-dicarboxylic acid was refluxed for 6 hours at 225-230° on an oil bath. The liquid acid remaining in the flask was distilled from a Würtz flask at 245-248° (711 mm). The yield totaled 4.2 g, or 78.6% of the theoretical. The literature gives the b.p. of cycloheptanecarboxylic acid as 248-250°.

d_4^{20} 1.0368; n_D^{20} 1.4722; MR_D 38.36; calculated 38.48.

According to N. D. Zelinsky [7], cycloheptanecarboxylic acid has d_4^{17} 1.0354 and n_D^{17} 1.4710.

0.2779 g substance: 0.6842 g CO_2; 0.2496 g H_2O. Found %: C 67.15; H 9.98. $C_8H_{14}O_2$.
Calculated %: C 67.60; H 9.86.

The acid was converted into an acid chloride by the action of phosphorus pentachloride, the acid chloride being added drop by drop to a chilled and concentrated solution of ammonia. The resultant amide had a m.p. of 193-194° after double recrystallization from dilute alcohol [5,7].

SUMMARY

1. ζ-Iodohexylmalonic ester has been synthesized by reacting hexamethylene iodide with sodium malonic ester.

2. Cyclization of ζ-iodomalonic ester by reacting it with sodium alcoholate in a 0.1-molar solution yielded cycloheptane-1,1-dicarboxylic ester, the yield being 34.7% of the theoretical.

3. Saponifying cycloheptane-1,1-dicarboxylic ester yielded cycloheptane-1, 1-dicarboxylic acid, which was decarboxylated to cycloheptanecarboxylic acid, identical with the acid previously described.

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Received September 16, 1950

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RESEARCH ON THE ISOMERIC TRANSFORMATIONS OF α-KETOLS

X. BENZYLACETYLCARBINOL

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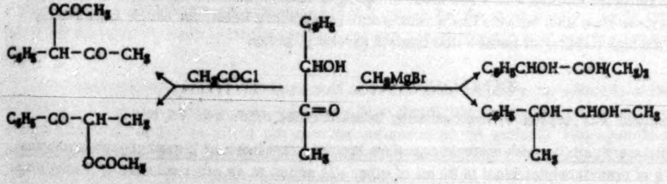
In 1934 A.E.Favorsky and T.I.Temnikova [1] discovered the extraordinary dynamicity of aliphatic-aromatic α-ketols, the example they investigated having been phenylacetylcarbinol.

They showed that when this carbinol was reacted with organomagnesium compounds and acid chlorides, the formation of the normal reaction products was parallelled by the formation of products whose structure was that of the isomeric ketol — methylbenzoylcarbinol.



In a series of papers that were a continuation of this research, it was shown that these properties occur particularly strikingly when the ketol contains a secondary alcoholic group alongside the aromatic ring and the acetyl group [2].

These peculiarities were not observed in the researches of A.E.Favorsky and his co-workers on diverse aliphatic ketols [3].

We were interested in learning how the C_6H_5 group affects the chemical properties of the ketocarbinol group, and, with this in view, in making a study of the behavior of an aliphatic-aromatic ketol whose C_6H_5 group is separated from the CHOH-CO-group by at least one carbon atom in these same reactions. The present paper is a report on our research on benzylacetylcarbinol (I), which can be readily prepared by the method described in a previous paper [4].

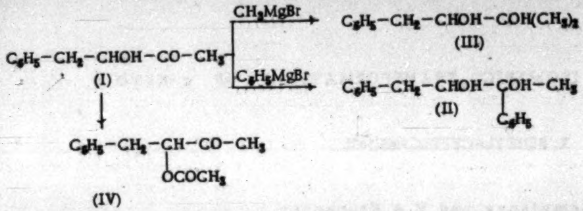
Our experiments have indicated that the reaction is normal when either C_6H_5MgBr or CH_3MgBr is used, the respective glycols: 1,3-diphenylbutanediol-2,3 (II), with a m.p. of 108-109°, and 4-phenyl-2-methylbutanediol-2,3 (III), with a m.p. of 63-64°, being produced.

The synthesis of the first glycol has been described in a previous paper [4]. The structure of the glycol synthesized by reacting benzylacetylcarbinol with methylmagnesium bromide, was established by oxidizing it with lead tetraacetate. Phenylacetaldehyde was identified as its semicarbazone, with a m.p. of 151-152°, acetone being identified as its p-nitrophenylhydrazone. 4-Phenyl-2-methylbutanediol had been described earlier by Lévy [5], who synthesized it by reacting the ethyl ester of α-hydroxy-β-phenylpropionic acid with methylmagnesium bromide and gave its m.p. as 64-65°.

The reaction of benzylacetylcarbinol with acetyl chloride was equally normal, yielding the acetic ether of benzylacetylcarbinol (IV): (see top of next page).

Thus benzylacetylcarbinol behaves like an aliphatic ketol in the foregoing reactions, in contrast to phenylacetylcarbinol.

In our previous papers we advanced hypothetical schemas for the mechanisms involved in the processes leading to the formation of anomalous reaction products. We see from the present research that introducing a methylene group between the phenyl ring and the ketol group completely annihilated the specific influence of the phenyl



upon the mobility of the carbinol hydrogen, which is transferred during the reaction, together with an electron pair, to the adjacent carbon atom of the carbonyl group. Apparently, it is the mobility of the hydrogen atom that is the basic factor governing the rearrangement of the molecule during its reaction with acid chlorides and organomagnesium compounds. It is worthy of note that in the molecular rearrangements of the bromoketones, occurring when the bromine in bromoketones is replaced by an acetoxy group and resulting in the formation of acetic ethers of the isomeric ketols, one of the factors determining the reconstruction during the reaction is also the mobility of the hydrogen atom in the α-position to the phenyl ring, as has been demonstrated in the researches of V.I.Veksler [6].

Benzylacetylcarbinol is a stable compound, no isomeric conversion to methylphenacetylcarbinol being observed when it is heated in alcoholic solution with a few drops of H_2SO_4 or when it is acted upon by alkalies in the cold. Thus here, too, benzylacetylcarbinol behaves like a representative aliphatic ketol, for which A.E.Favorsky [3] established the rule of the high stability of isomers that contain an acetyl group.

EXPERIMENTAL

The benzylacetylcarbinol was prepared by hydrogenating benzalacetone oxide over Pd/Ni [4].

1. Reaction of benzylacetylcarbinol with methylmagnesium bromide (synthesis of 2-methyl-4-phenylbutanediol-2,3). A solution of 5 g of benzylacetylcarbinol in 30 ml of ether was added to an ether solution of methylmagnesium bromide, prepared from 3 g of magnesium. The mixture was set aside for 24 hours, after which the organomagnesium complex was decomposed with water without any acid being added. After the ether had been driven off, the colorless solid residue was recrystallized from petroleum ether; this yielded minute white crystals, shaped like pointed feathers. M.p. 63-64°. Yield: 4.4 g (80%).

0.1062 g substance: 0.2846 g CO_2; 0.0688 g H_2O. 0.1178 g substance: 0.3159 g CO_2; 0.0766 g H_2O. 0.0783 g substance: 17.2 g benzene: Δt 0.134°; 0.0738 g substance: 129 ml CH_4 (19.5°; 759.5 mm). 0.0661 g substance: 17.6 ml CH_4 (19.5°; 759.5 mm). Found %: C 73.13, 73.18; H 7.25, 7.18. M 174.3; active H 1.97, 1.94. $C_{11}H_{16}O_2$. Calculated %: C 73.29; H 7.11; M 180.13; active H 2.00.

Oxidation of the glycol with lead tetraacetate. 7 g of lead tetraacetate was added to 1.5 g of the glycol dissolved in 18 ml of glacial acetic acid, and the mixture was heated to 55°. When the crystals of lead tetraacetate had disappeared, heating was stopped, and a saturated solution of K_2CO_3 (50% of what would be required to neutralize the acetic acid) was slowly added to the cooled mass. The oxidation products were driven off with steam to identify them; the first portion of the distillate, collected in a solution of p-nitrophenylhydrazine, yielded a yellow crystalline precipitate. The crystals had a m.p. of 146-147° after recrystallization, which is the figure given for the p-nitrophenylhydrazone of acetone (the mixed melting point with a known sample exhibited no change).

As distillation was continued, yellowish drops passed over together with the steam. The distillate was collected in a semicarbazide solution, the reaction with semicarbazide being instantaneous. The m.p. of the crystals was 151-152° after they had been recrystallized from dilute alcohol. The mixed melting point with a known preparation of the semicarbazone of phenylacetaldehyde exhibited no depression. Acetone was recovered from the semicarbazide mother liquor in the usual manner and identified as its p-nitrophenylhydrazone.

In this case, therefore, we have been able to identify phenylacetaldehyde by oxidizing a glycol with a benzyl radical; in the previous experiments [4,7], apparently, the aldehyde was polymerized when the oxidation products were distilled from an alkaline medium, though they are fairly stable in an acid medium.

2. Reaction of benzylacetylcarbinol with acetyl chloride (synthesis of the acetic ether of benzylacetylcarbinol). A solution of 2.4 g of the ketol in 15 g of pyridine was chilled to 0° and 2 g of acetyl chloride (a 70% excess) was added. The mixture was set aside overnight, after which it was poured into 80 ml of 10% H_2SO_4. An oily layer was formed, which was extracted with ether. After drying with $CaCl_2$ and driving off the ether, the residue

was distilled in vacuo, all of the substance passing over, except for a few drops, at 107-108° and 1 mm. The yield was 78%. The colorless liquid reduced Fehling's solution when boiled with it.

d_4^{20} 1.0833; n^{20} 1.5000; MR_D 55.96. Calculated 55.68.
0.1116 g substance; 0.2853 g CO_2; 0.0704 g H_2O. 0.1279 g substance: 0.3267 g CO_2; 0.0799 g H_2O.
Found %: C 69.77, 69.73; H 7.06, 6.98. $C_{12}H_{14}O_3$. Calculated %: C 19.87; H 6.85.

The synthesized acetic ether was converted into a glycol to establish the structure and individuality of the substance.

An ether solution of 2.8 g of the acetyl derivative was added drop by drop, with stirring and chilling, to an ether solution of methylmagnesium bromide, prepared from 1.9 g of Mg. The rest of the processing was the usual one. This resulted in the recovery of a crystalline substance with a m.p. of 63-64°, whose mixed melting point with the glycol with a m.p. of 63-64°, synthesized from benzylacetylcarbinol and CH_3MgBr, exhibited no depression. The glycol with a m.p. of 63-64° was the sole reaction product.

3. Endeavors to isomerize benzylacetylcarbinol in an acid and an alkaline medium were made in the usual manner [2,3]. In both cases the substance recovered was converted into a glycol by reacting it with C_6H_5MgBr, a single product, with a m.p. of 108-109° being isolated, which exhibited no depression with the known glycol possessing the same melting point, prepared from benzylacetylcarbinol—1,3-diphenylbutanediol-2,3.

SUMMARY

1. It has been shown that the reaction of benzylacetylcarbinol with methylmagnesium bromide yields only a single glycol — 2-methyl-4-phenylbutanediol-2,3, which has the same structure as the initial ketol. The only product of the reaction between benzylacetylcarbinol and acetyl chloride is an acetic ether corresponding to the initial ketol.

2. Benzylacetylcarbinol has been used to define more precisely the influence of the phenyl group upon the properties of the ketocarbinol group, and it has been shown that introducing a methylene group between the phenyl and the CHOH-CO group nullifies the specific influence of the aromatic ring upon the mobility of the hydrogen atom in the carbinol group that has been observed in research upon a number of aliphatic—aromatic ketols that have aryl groups directly adjacent to the ketol group.

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Received September 20, 1950.

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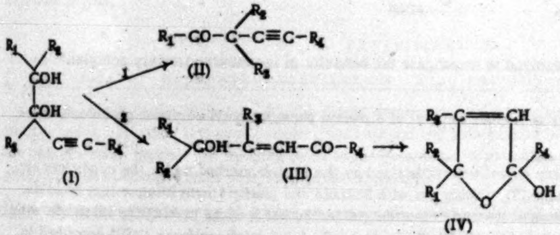
TRANSFORMATIONS OF SECONDARY-TERTIARY α-ACETYLENIC GLYCOLS PRODUCED BY MERCURY SALTS

I. 1,2,4-TRIPHENYLBUTYN-3-DIOL-1,2

E.D. Venus-Danilova and V.M. Albitskaya

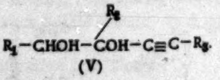
It has been shown in a series of papers on the transformations of ditertiary α-glycols (pinacols) of the acetylene series (I) that take place in the presence of sulfuric acid that these glycols are converted into acetylenic ketones (II) [1] or are isomerized into tertiary ethylenic γ-ketols (III), which can then be cyclized to substitution derivatives of hydroxydihydrofuran (IV) [2]:



Some acetylenic pinacols [3] are capable of both of these transformations – the acetylenic–allenic (1) and the pinacol (2) – inasmuch as their conversion products have been found to contain acetylenic ketones (II) (Transformation 1), unsaturated γ-ketols (III), and products of the ketols' cyclization – substituted hydroxydihydrofurans (IV) (Transformation 2).

A detailed investigation of these conversions, using eight pinacols, has shown that the quantitative proportions and the stability of the transformation products are directly related to the structure of the initial glycol, i.e., to the nature and the arrangement of the substituents attached to the hydroxylated carbon atoms of the pinacol.

In connection with these behavior patterns in the transformations of acetylenic pinacols, we felt it was worthwhile to undertake an investigation of the rearrangements under identical conditions of the secondary – tertiary acetylenic α-glycols (V), whose structure differs from that of the pinacols (I) studied in that they have a hydrogen atom attached to the first hydroxylated carbon atom instead of one of the radicals:



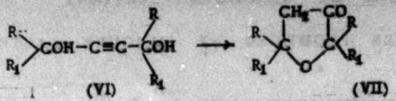
$$R_1-CHOH-\overset{R_2}{C}OH-C\equiv C-R_3.$$

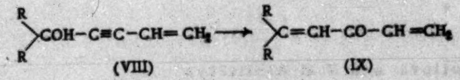
(V)

Preliminary experiments, made with diphenyl phenylethynyl ethylene glycol (1,2,4-triphenylbutyn-3-diol-1,2) (V. $R_1=R_2=R_3=C_6H_5$), have shown that when this glycol is reacted with 30, 37, and 42% of sulfuric acid, no products are formed, neither those of a pinacol conversion nor those of an acetylenic–allenic rearrangement; part of the initial reagents is recovered unchanged and part undergoes carbonization.

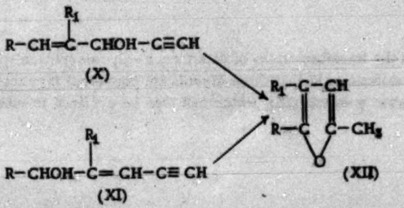
Then we investigated the behavior of this glycol with mercury salts, in the light of the data in the literature. It is asserted therein that mercury salts can give rise to isomerization of acetylenic glycols and alcohols, in addition to hydrating them, in certain cases.

The acetylenic γ-glycols (VI), for instance, are converted into substitution derivatives of ketohydrofuran (VII) [4]; vinylacetylenic alcohols (VIII) are converted into divinyl ketones (IX) [5]; and some ene-yne alcohols (X, XI) are isomerized to substitution derivatives of furan (XII) [6]:


(VI) (VII)


(VIII) (IX)

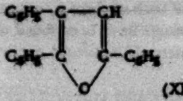
$R_2C(OH)-C\equiv C-CH=CH_2 \longrightarrow R_2C=CH-CO-CH=CH_2$


(X) (XI) (XII)

In the light of these findings, we resolved to investigate the behavior of secondary—tertiary acetylenic α-glycols (V) with mercury salts.

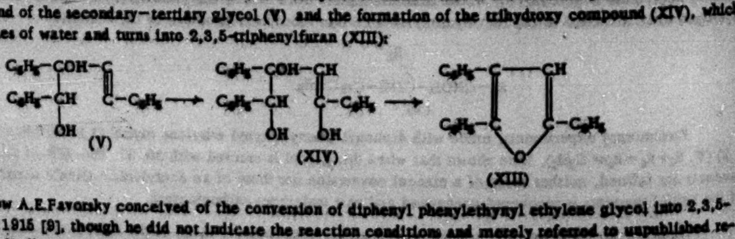
The first reaction we selected for this purpose was that of diphenyl phenylethynyl ethylene glycol and mercuric chloride.

The diphenyl phenylethynyl ethylene glycol was synthesized by the Iotsich method under the conditions employed by Yu. S. Zalkind and E. E. Martinson [7], starting out with benzoin and phenylethynylmagnesium bromide. Heating the glycol with an alcoholic solution of mercuric chloride yielded 80% of a white crystalline substance with a m.p. of 91°, which proved upon analysis and from its properties to be the 2,3,5-triphenylfuran (XIII) described in the literature [8]:


(XIII)

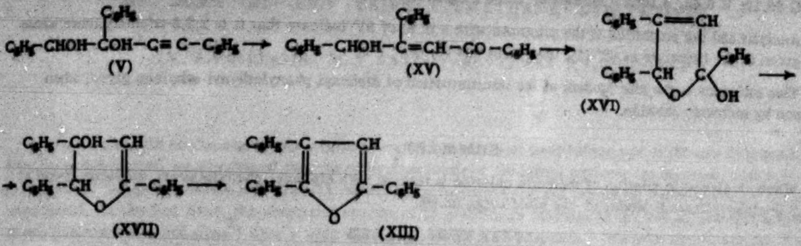
The conversions of secondary—tertiary acetylenic α-glycols into substitution derivatives of furan by the action of mercury salts has not been described in the literature. As has been noted, however, there are reports [6] of the isomerization of unsaturated alcohols that contain both ethylenic and acetylenic bonds into substitution derivatives of furan when they are heated with mercuric sulfate or mercuric oxide and boron trifluoride in methanol.

As for the mechanism of this transformation, it is simplest to assume that it involves the partial hydration of the acetylenic bond of the secondary—tertiary glycol (V) and the formation of the trihydroxy compound (XIV), which loses two molecules of water and turns into 2,3,5-triphenylfuran (XIII):


(V) (XIV) (XIII)

This is how A.E.Favorsky conceived of the conversion of diphenyl phenylethynyl ethylene glycol into 2,3,5-triphenylfuran in 1915 [9], though he did not indicate the reaction conditions and merely referred to unpublished research by N.V. Palladin.

But in view of the mobility of the hydroxyl group at the α-position to the triple bond [10] and the ability of ditertiary acetylenic α-glycols to enter into an acetylenic–allenic rearrangement [11,2,3], which A. N. Elizarova and I.N. Nazarov [5] believe can also be effected by mercury salts, we may state that in our case the furan compound was formed from the unsaturated secondary γ-ketol (XV) via the hydroxyhydrofuran (XVI), which is converted into a substitution derivative of furan as the result of an allylic rearrangement (XVII) and dehydration:



This reaction will have to be checked for other glycols of analogous structure, and their behavior toward sulfuric acid to determine the feasibility of an acetylenic–allenic rearrangement for them, if we are to obtain a final solution of the problem of the way in which 2,3,5-triphenylfuran is produced from diphenyl phenylethynyl ethylene glycol.

EXPERIMENTAL

I. Synthesis of Diphenyl Phenylethynyl Ethylene Glycol (1,2,4-Triphenyl-butyn-3-diol-1,2)

According to the literature [7], the glycol was synthesized from phenylacetylene, magnesium, and benzoin, its m.p. being 175° after recrystallization from benzene and then from ethyl alcohol. The yield was 58%, based on the benzoin used. Neither the melting point of the glycol nor its properties differed from those of the diphenyl phenylethynyl ethylene glycol described in the literature.

II. Action of Mercuric Chloride upon Diphenyl-Phenylethynyl Ethylene Glycol

Experiment 1. A saturated alcoholic solution of the glycol (1 g of the glycol in 15 ml of 96% ethyl alcohol), to which 0.3 g of mercuric chloride had been added, was heated for 8 hours in a sealed tube on a boiling water bath. A yellowish mass formed at the bottom of the tube, the alcoholic solution being threaded through by a white crystalline substance. The amorphous mass was separated, washed twice with hot water to remove the mercuric chloride, and recrystallized from alcohol. This yielded 0.2 g of a finely crystalline white powder with a m.p. of 89°. 0.6 g of a white crystalline product was filtered out of the alcoholic layer; its m.p. was 90° and it exhibited no depression of the mixed melting point with the substance whose m.p. was 89°, which had been isolated from the deposit on the bottom of the tube.

Experiment 2. A saturated alcoholic solution of the glycol (1 g of the glycol in 15 ml of ethyl alcohol), containing 0.6 g of mercuric chloride, was heated for 8 hours in a sealed tube on a boiling water bath. As in Experiment 1, we secured 0.15 g of a substance with a m.p. of 89° and 0.7 g of a substance with a m.p. of 90°, suspended in the alcohol.

Experiment 3. 0.9 g of mercuric chloride and a saturated alcoholic solution of the glycol (1 g of the glycol in 15 ml of 96% ethyl alcohol) were heated together for 6 hours in a sealed tube at 110-115°. This yielded a white crystalline substance, which filled the entire tube. The substance weighed 0.85 g and had a m.p. of 91° after washing with hot water and recrystallization from alcohol.

The experimental results are summarized in the following table:

Test No.	Glycol (g)	Mercuric chloride, g	Heating time, hrs	Heating temp.	Yield	
					g	%
1	1	0.3	8	100°	0.8	85.1
2	1	0.6	8	100°	0.85	90.4
3	1	0.9	6	110-115	0.85	90.4
	3	1.8			2.5	88.6

We see that the product yield is unaffected by any change in the amount of mercuric chloride used, the heating time, or the temperature. A total of 2.5 g of the substance was secured, its m.p. being 91° after another recrystallization.

The substance with a m.p. of 91° is freely soluble in ether and benzene, but less so in alcohol. It decolorizes a chloroform solution of bromine and an aqueous solution of potassium permanganate when heated in them; it contains neither a hydroxyl nor a carbonyl group; and it colors strong sulfuric acid a deep red, the color disappearing when the acid is diluted with water.

0.1037 g substance: 0.3386 g CO_2; 0.0510 g H_2O. Found %: C 89.05; H 5.46. $C_{22}H_{16}O$. Calculated %: C 89.19; H 5.40. 0.1051 g substance: 12.96 g C_6H_6: Δt 0.14°. Found: M 281. $C_{22}H_{16}O$. Calc.: M 296.

Analysis and the properties of the substance with a m.p. of 91° indicate that it is 2,3,5-triphenylfuran, whose m.p. is given in the literature as 92° [8]. The yield was 88.6%.

This substance is the sole product of the transformation of diphenyl phenylethynyl ethylene glycol when acted upon by mercuric chloride.

SUMMARY

When an alcoholic solution of mercuric chloride is reacted with diphenyl phenylethynyl ethylene glycol at 100°, 2,3,5-triphenylfuran is produced the yield being 88.6%.

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Received October 11, 1950

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INVESTIGATION OF THE ABSORPTION SPECTRA OF SOME DI- AND TRIPHENYLMETHANE DERIVATIVES

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In our research on the absorption spectra of some derivatives of naphthalene and of the azo dyes synthesized from these derivatives, we discovered that the absorption bands of the initial products are repeated, with a few deviations, in the spectra of the azo dyes [1]. With a view to confirming and extending this observation, we have investigated, for the first time, the absorption spectra of 15 genetically interrelated di- and tri-phenylmethane compounds (intermediates and dyes[*]) over a wide wavelength range (210-650 mμ). We were also interested in tracing the ways in which the absorption spectra evolve when the structure of a substance is changed.

The spectrophotometric measurements were made with a Type SF-1 photoelectric device; the effective slit width was about 1 mμ at 250 mμ. This enabled us to resolve the fine structure of the absorption bands whenever the distances between maxima were of that order of magnitude. The absorption of the solvent has been excluded from all our findings. With the sole exception of dimethylaniline, all the substances were specially synthesized and thoroughly purified (recrystallization from various solvents and distillation in vacuo). Identical concentrations were used in our research, these concentrations being later recalculated into molar concentrations (C_m); the same solvent (ethyl alcohol; pH = 8) was employed in every case, as a rule. The absorption spectra were measured for freshly prepared solutions, as well as for the solutions after they had stood in the dark for 24 hours. The position of the bands remained constant, only their intensity changing slightly; hence, the substances were sufficiently stable under the experimental conditions we employed.

Diphenylmethane (I) [2-9] and triphenylmethane (II) [4,6,8,9-11][**] were the parent substances of all the compounds tested. The absorption spectra of these substances have a single absorption band that exhibits fine structure (Figure 1). In both of these compounds, the center of gravity of each band (262 mμ), as well as the location of the fine-structure bands and their intensity ratios, coincide nearly completely.

The absorption spectra of diphenylcarbinol (III) and triphenylcarbinol (IV) [4,12-14] retain the fine structure of the absorption band. The spectra of both carbinols are pretty much alike, differing from the spectra of the respective hydrocarbons (I) and (II) in that they exhibit a decrease in the number of the fine-structure bands and a change in the intensity ratios of these bands.

Comparison of the spectra (I), (II), (III), and (IV) indicates that the substitution of a benzene ring for the hydrogen atom attached to the central carbon atom increases the intensity of the absorption band (ε), while substituting a hydroxyl group for the hydrogen atom lowers the intensity and results in widening of the elementary bands.

When two dimethylamino groups are introduced into diphenylmethane and one, two, or three dimethylamino groups into triphenylmethane, the absorption band of the initial substance is preserved in the absorption spectra of these amines, while a new, though rather weak, band, at the longer wavelength of 300 mμ distinctly makes its appearance (Figures 3 and 4, and Table 1). It should be noticed that dimethylaniline (V) [3,6,15-17] has an absorption spectrum whose band positions and intensity ratios are quite close to those of the spectra of the tested di- and triphenylmethane amines (Fig. 3, Table 1). Increasing the number of dimethylamino groups in the compounds in question does not cause any new band to appear, merely promoting the reappearance of the fine structure of the already existing shortwave band, which is absent in the compound (VII) and distinctly visible in (IX), and increasing the intensity of both absorption bands [compare spectra (VII), (VIII), and (IX).]

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[*] Some of the substances we have investigated have been analyzed spectroscopically more than once in the past, the results agreeing with those obtained in our research (as in di- and triphenylmethane and the triphenylmethane dyes — malachite green and crystal violet), but no systematic investigations have been carried out with the objective set forth above. There are no figures in the literature for several of these substances (VI, VII, VIII, IX, and X).

[**] The absorption curve rises at $\lambda < 210$ mμ in all the substances, due to the presence of a band in the 200 mμ region.

The intensity ratios of the shortwave to the longwave bands diminishes in that order; however, the growth of the shortwave band outstripping that of the longwave one.

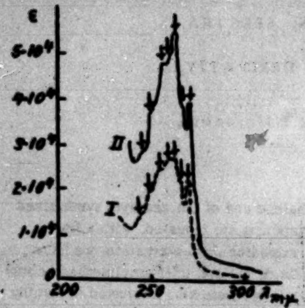


Fig. 1. Absorption spectra: I) diphenylmethane; II) triphenylmethane.

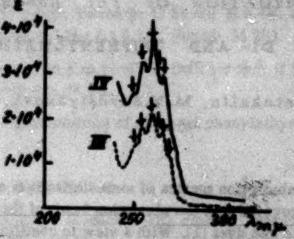


Fig. 2. Absorption spectra: III) diphenylcarbinol; IV) triphenylcarbinol

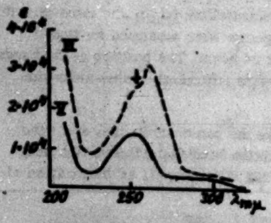


Fig. 3. Absorption spectra: V) di-m-phenylaniline; VI) tridiamino-diphenylmethane.

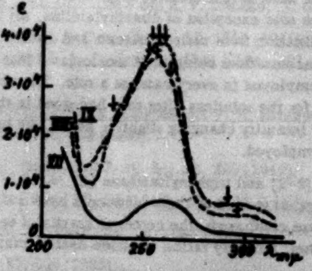


Fig. 4. Absorption spectra: VII) Dimethyldiaminotriphenylmethane; VIII) leucomalachite green; IX) leucocrystal violet.

The carbinol derivatives of part of the amines discussed above exhibit optical properties that are unexpectedly somewhat different from those of the amines proper. To be sure, the spectra of the carbinols (X), (XI), and (XII) [13] (Figure 3 and Table 1)[(XI) and (XII) are the carbinol bases of malachite green and crystal violet], like those of the initial amines, retain two absorption bands at the same wavelengths; the transition from the diphenylmethane carbinols to the triphenylmethane carbinols and an increase in the latter's dimethylamino groups, however, cause a decrease rather than an increase in the intensity of both bands, to begin with, and second, does not cause a more distinct manifestation of the fine structure of the shortwave band, as was the case with the amines.

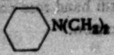
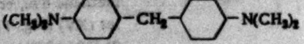
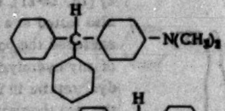
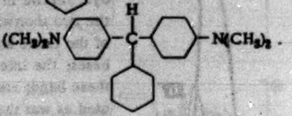
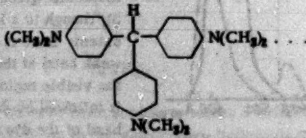
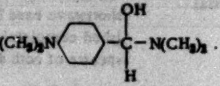
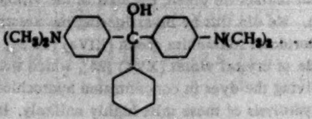
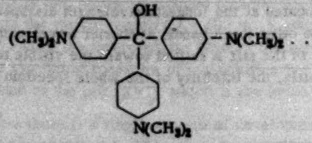
Thus, the absorption spectra of the investigated di- and triphenylmethane hydrocarbons [di- and triphenylmethane, (I) and (II)] and their hydroxyl derivatives [di- and triphenylcarbinol, (III) and (IV)] have one distinct absorption band that possesses fine structure. The introduction of dimethylamino groups into these compounds preserves this shortwave band in the spectra of the resultant substances (the fine structure of the band being obliterated) and results in the appearance of a weak new band at longer wavelengths.

This picture grows much more complicated when we explore the absorption spectra of colored salts or dyes, derived from the intermediates mentioned above.

The spectrum of the colored salt of tetramethyldiaminodiphenylmethane (XIII) [18,19], prepared from the carbinol (X), retains both bands of the original carbinol; moreover, a new low intensity band appears in the longwave region of the spectrum (Figure 6 and Table 2).

Malachite green (XIV) [13, 19-22] was tested at pH values that made hydrolysis impossible [23], resulting in the formation of an equilibrium mixture of the dye and the carbinol; thus what we measured was a solution of the dye proper.

TABLE 1

Substance[*]	C_m	I λ	I $\varepsilon\cdot10^{-4}$	II λ	II $\varepsilon\cdot10^{-4}$	$\frac{\varepsilon_1}{\varepsilon_2}$
(V) 	–	251	1.34	290	0.25	5.3
(VI) 	$7.8\cdot10^{-5}$	(255) 262	(2.6)[**] 3	300	0.42	7.1
(VII) 	$6.1\cdot10^{-5}$	260	0.73	300	0.094	7.7
(VIII) 	$6.0\cdot10^{-5}$	(260) 262 (268)	(3.47) 3.52 (3.2)	300	0.53	6.6
(IX) 	$5.3\cdot10^{-5}$	(240) 260.0 262.5 265.0	(2.32) 3.78 3.84 3.82	298	0.74	5.1
(X) 	$7.4\cdot10^{-5}$	267	2.48	300	0.33	–
(XI) 	$5.8\cdot10^{-5}$	(260) 264	(1.4) 1.58	300	0.2	–
(XII) 	$5.0\cdot10^{-5}$	260	0.24	300	0.11	–

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[*] Spectra (V) through (IX) were explored in ethyl alcohol mixed with a few drops of a 10% hyposulfite solution; (X) was explored in ethyl alcohol, pH = 8.0; (XI) and (XII) in an alcoholic–alkaline medium, pH = 12.0, the alkali being added until dissociation of the carbinols was prevented, resulting in formation of the colored dye ion.

[**] The figures for weak maxima are given in parentheses.

The spectrum of malachite green (Figure 7 and Table 2) retains both of the shortwave bands in the spectrum of the leuco and carbinol bases (VIII) and (IX) from which it can be produced. But the dye exhibits some displacement of the shortwave band toward the ultraviolet, compared to the spectra of these substances, while the longwave band is displaced toward the visible region; we discovered a redistribution of the intensities of these bands: the intensity of the shortest wavelength band dropped markedly, while that of the longer wavelength band rose considerably (Table 3); what is more, two new bands appeared in the visible region of the dye's spectrum.

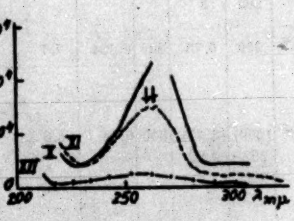

Fig. 5. Absorption spectra: X) tetramethyldiaminodiphenylcarbinol; XI) carbinol base of malachite green; XII) carbinol base of crystal violet.

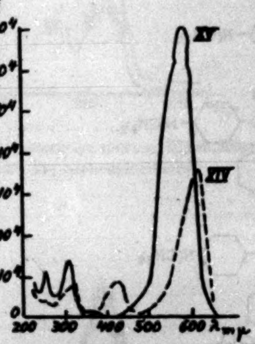

Fig. 7. Absorption spectra: XIV) malachite green; XV) crystal violet.

Another triphenylmethane dye, crystal violet (XV) (Fig. 7 and Table 2) [13, 19-21], which was also tested at a pH that excluded the possibility of any hydrolysis of the dye, retains in its spectrum the two shortwave bands of the leuco and carbinol bases; the intensities of these bands are redistributed as was the case with malachite green (Table 3), though to a lesser extent; there is a very weak band at the edge of the visible region, which is followed by the strong band of the dye proper. The fine structure of the shortwave band has vanished completely in the spectra of both dyes.

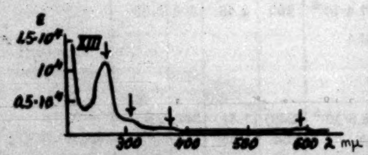

Fig. 6. Absorption spectra: XIII) salt of tetramethyldiaminodiphenylcarbinol.

We then tried to track down the genesis of the second absorption band of malachite green, located in the visible region (λ = 425 mμ). We did this by investigating the absorption of the dihydrochloride of malachite green (XIVa) [13,24] and the trihydrochloride of crystal violet (XVa) [25], which were prepared by dissolving the dyes in concentrated hydrochloric acid, which made hydrolysis of these salts highly unlikely. In the absorption spectrum of the salt (XIVa) only the band of the original dye located at the longest wavelength disappears, the positions of the other three bands, at shorter wavelengths, suffering no substantial changes; merely the longest wavelength band of the salt is shifted toward the visible region (λ = 442 mμ), compared to the corresponding band in the dye. Lastly, the intensity of the whole spectrum drops sharply (Figure 8 and Table 4).

In the spectrum of the salt (XVa) the longwave band of crystal violet also vanishes, together with the weak band located at the boundary of the visible region (λ = 360 mμ).* At the same time, a new band arises in the visible region (λ = 435 mμ); the other two shortwave bands retain their position (Figure 8 and Table 4).

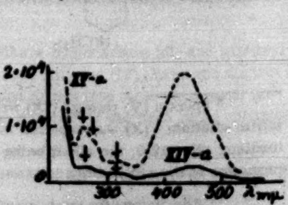

Fig. 8. Absorption spectra: XIVa) malachite green dihydrochloride; XVa) crystal violet trihydrochloride.

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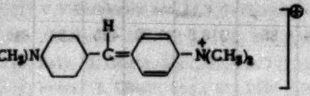
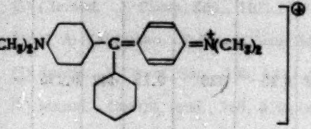
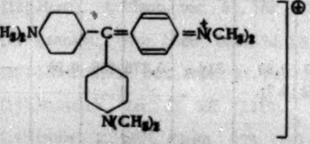
* The disappearance of this band when a salt of crystal violet is formed disproves the assumption of its common origin with the intermediate band of malachite green and the longwave band of diaminotriphenylcarbinol (XVI).

TABLE 2

Substance	Cm	pH	I		II		III		IV	
			λ	$\varepsilon\cdot10^{-4}$	λ	$\varepsilon\cdot10^{-4}$	λ	$\varepsilon\cdot10^{-4}$	λ	$\varepsilon\cdot10^{-4}$
(XIII) 	$6.9\cdot10^{-5}$	Ethyl alcohol 8.0*	265	1.14	300	6.2	(340)	(0.058)	595	0.03
(XIV) 	$5.4\cdot10^{-5}$	Buffer 4.2	249	0.35	316.5	0.82	425	0.86	620	3.44
(XV) 	$4.9\cdot10^{-5}$	Buffer 5.67	250	1.09	303	1.37	(360)	(0.13)	589 (560	6.97 5.68)

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* We have been unable to select a buffer for this dye which would dissolve it completely and permit adequate transmission in the ultraviolet; hydrolysis may take place in ethyl alcohol, so that the figures given for ε are merely approximate.

TABLE 3

Intensity Ratios of Two Shortwave Absorption Bands

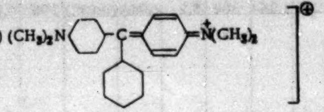
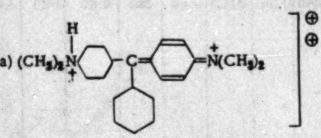
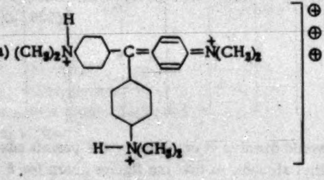
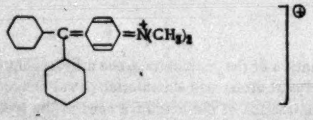
Substance	(VIII)	(XI)	(XIV)	(IX)	(XII)	(XV)
$\frac{\varepsilon_1}{\varepsilon_2}$ . . .	6.64	7.9	0.43	5.2	2.0	0.8

Formation of the malachite green dihydrochloride (XIVa) and crystal violet trihydrochloride (XVa) is accompanied by elimination of the longwave band in the spectra of the initial dyes, owing to the interaction of the dimethylamine groups of these dyes with the hydrogen ions and their conversion into groups with an electron configuration that resembles that of the optically inactive methyl group. The structure of these salts is like that of the salt of dimethylaminotriphenylcarbinol (XVI) [13,26] (Table 4), which contains one postively charged dimethylamino group, the spectrum of which we know has only one absorption band in the visible region (λ = 480 mμ), whose position is close to that of the longwave bands of salts (XIVa) and (XVa) and of the intermediate band of malachite green. The conclusion that thrusts itself upon one, therefore, is that the absorption spectrum of malachite green contains not only the bands of the leuco and carbinol bases, but also the band of the salt (XVI), which is the foundation of the dye.

Thus there is a single pattern of development of the absorption spectra that is common to all of the three genetic series constituted: 1) by the salt of tetramethyldiaminodiphenylcarbinol (XIII); 2) malachite green (XIV); and 3) crystal violet (XV), and to the salts of the last two and the respective leuco and carbinol bases of these dyes: with a few exceptions, the dye's absorption spectrum repeats the bands of the initial products; moreover, the dyes' spectra repeat only the strong absorption bands, located in the visible region as a rule, that belong to them.

Another rule observed by us appears with even greater distinctness in the absorption spectra of phenylmethylpyrazolone and its various derivatives. Phenylmethylpyrazolone exhibits in its spectrum one strong absorption band at 246 mμ; in all the compounds, without exception, that were synthesized by reacting phenylmethylpyrazolone with aldehydes, nitroso and diazo compounds (a large number of substances, some of which had highly complicated structures, was investigated [27], the absorption band of phenylmethylpyrazolone is preserved, a new band belonging to the given compound making its appearance in the longwave region, and the intensity of the shortwave band being somewhat less than that of the longwave one and lower than in the original phenylmethylpyrazolone.

TABLE 4

Substance*	I		II		III		IV	
	λ	$\varepsilon \cdot 10^{-4}$	λ	$\varepsilon \cdot 10^{-4}$	λ	$\varepsilon \cdot 10^{-4}$	λ	$\varepsilon \cdot 10^{-4}$
(XIV) 	249	0.35	316.5	0.82	425	0.86	620	3.44
(XIVa) 	262	0.25	320	0.12	442	0.275	—	—
(XVa) 	259 (280)	0.99 (0.7)	314	0.375	436	0.98	—	—
(XVI) 	250 (285)	—	333	—	480	—	—	—

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* (XIVa) and (XVa) were explored in 30% hydrochloric acid, while (XVI) was explored in dilute hydrochloric acid.

The following considerations may be put forward in connection with the genesis of the absorption bands in the spectra of the substances tested. As we know, each electronic band arises as the result of a shift of the molecule from the ground state to an excited state. At that instant only a single absorption band arises in the spectrum, since the molecule can effect only a single energy change at a time. Hence the spectrum of a compound that exhibits several absorption bands is a statistical picture of various energy changes.

Whenever the location of a spectrum band of a dye (say, the shortwave band of crystal violet) coincides with that of the original compound (say, the carbinol base of crystal violet), it may be assumed that the excitation energies responsible for the appearance of these bands are the same. Hence, the energy changes of the original substances are reproduced in the dyes. The intensity of the absorption bands is determined by the probability of the energy changes.

SUMMARY

1. Investigation of the absorption spectra of numerous diphenylmethane and triphenylmethane compounds, as well as of phenylmethylpyrazolone and of various dyes synthesized from these substances shows that the absorption bands of the original substances are repeated in the spectra of the dyes.

2. It has been established that this phenomenon is accompanied by a certain shift of the position of the shortwave bands (compared to the initial products) in the dye spectra and by a redistribution of their intensities.

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Received July 7, 1950

DERIVATIVES OF ACETYLENE

138. HETEROCYCLIC COMPOUNDS

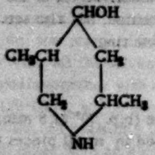
XIV. Synthesis of Secondary γ-Piperidols by Reducing γ-Piperidones

I.N.Nazarov and V.A.Rudenko

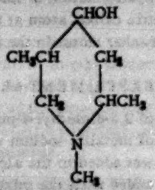
The high physiological activity of many natural esters of the secondary γ-piperidinic alcohols (cocaine, atropine, scopolamine, and the like) and of synthetic preparations of similar structure, which have been widely employed as anesthetics and mydriatics (eucaine, euphthalmine), is largely responsible for the undiminished interest in this group of compounds. The compounds of this type that have been synthesized and tested recently include substances that are highly active spasmolytically [1] and mydriatically [2], possess strong curarelike activity [3], and can be employed as substitutes for quinidine [4]. The secondary alcohols of the γ-piperidine series may also be intermediate products in the synthesis of substitution derivatives of the γ-aminopiperidines that act as spasmolytics.

We were, of course, interested in synthesizing the secondary γ-alcohols of the piperidine series by reducing the respective γ-piperidones, which have become readily available in wide variety as the result of our discovery of a simple method of producing them by reacting vinyl allyl ketones with ammonia and primary amines [5].

Reducing 2,5-dimethyl-4-piperidone with metallic sodium in absolute alcohol yielded 2,5-dimethyl-4-piperidol (I) with a m.p. of 96-97°. A Raney nickel catalyst hydrogenates 2,5-dimethyl-4-piperidol to a mixture of isomeric 2,5-dimethyl-4-piperidols, the bulk of which is the isomer (II) with a m.p. of 138°:

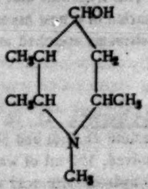


(I) M.p. 96-97°;
(II) M.p. 138°;



(III) B.p. 80-81° at 5 mm;
picrate m.p. 138-139°;

(IV) B.p. 87-88° at 7 mm;
picrate m.p. 116-118°.



(V) M.p. 77-79°;
picrate m.p. 181-182°.

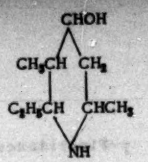
(VI) B.p. at 4 mm 92-93°;
picrate m.p. 104-106°.

Reducing 1,2,5-trimethyl-4-piperidone with metallic sodium in absolute alcohol yielded liquid 1,2,5-trimethyl-4-piperidol (III) with a b.p. (5 mm) of 80-81°; the picrate m.p. was 138-139°. Hydrogenation of 1,2,5-trimethyl-4-piperidone at room temperature with a platinum catalyst likewise yielded liquid 1,2,5-trimethyl-4-piperidol (IV) with a b.p. (7 mm) of 87-88°; the picrate m.p. was 116-118°.

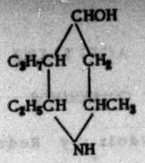
Reducing 1,2,3,6-tetramethyl-4-piperidone with metallic sodium in absolute alcohol yielded 2 isomers: a crystalline isomer with a m.p. of 77-79° (V) and a liquid isomer with a b.p. at 4 mm of 92-93° (VI). The isomeric alcohols were separated and then isolated in the pure state by fractionally crystallizing their picrates, followed by decomposing the individual picrates with a concentrated potash solution.

Reducing 2,5-dimethyl-6-ethyl-4-piperidone with metallic sodium in absolute alcohol under the same conditions likewise yielded a mixture of isomeric alcohols, from which we were able to isolate only one crystalline 2-methyl-6-ethyl-5-propyl-4-piperidol (VIII) with a m.p. of 123°, as in the previous test.

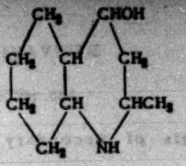
Successive fractional crystallization of the mixture of isomeric alcohols produced by reducing 2-methyl-4-ketodecahydroquinoline with metallic sodium in alcohol yielded 2 crystalline isomers of 2-methyl-4-hydroxydecahydroquinoline, with a m.p. of 111-113° (IX) and 185-186° (X):



(VII) M.p. 136-137°

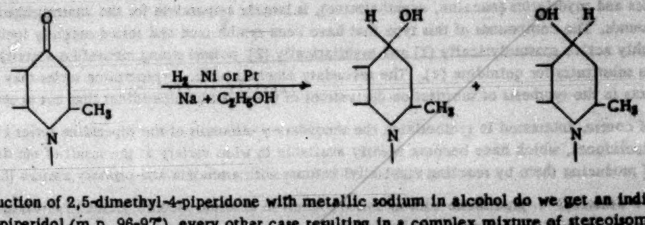


(VIII) M.p. 123°



(IX) M.p. 111-113°
(X) M.p. 185-186°

Thus, whether the substitution derivatives of γ-piperidones are reduced with metallic sodium in alcohol or catalytically hydrogenated with Ni and Pt catalysts, we usually obtain a mixture of stereoisomeric γ-piperidols, their proportions varying widely with the reaction conditions:



Only in reduction of 2,5-dimethyl-4-piperidone with metallic sodium in alcohol do we get an individual 2,5-dimethyl-4-piperidol (m.p. 96-97°), every other case resulting in a complex mixture of stereoisomers, this being particularly true when the carbonyl group is reduced in γ-piperidones that contain three or more substituents attached to the piperidine ring. This indicates that the hydrogenation of substitution derivatives of the γ-piperidones not only results in the formation of a new asymmetric carbon atom at the 4 position, but also sets up a different spatial arrangement of the substituents attached to the other atoms in the piperidine ring.

EXPERIMENTAL

2,5-Dimethyl-4-piperidol. 1) 12.7 g of 2,5-dimethyl-4-piperidone (b.p. 70° at 8 mm; n_D^{22} 1.4690) was dissolved in 350 ml of absolute alcohol and 35 g of metallic sodium was added in small pieces to the solution. After all the sodium had dissolved, 100 ml of water was added to the alcoholate, and then the mixture was stirred while 150 ml of concentrated hydrochloric acid was added until the mixture's reaction was acid. After the alcohol had been driven off, the salt solution was evaporated in a pan on a water bath, the sodium chloride being filtered out while hot. The filtrate (totaling about 150 ml) was saturated with alkali and extracted four times with ether. The ether solution was dried with calcined potash. After the ether had been driven off, the residue was distilled in vacuo (b.p. 85° at 4 mm), solidifying rapidly in the receiver. This yielded 9.5 g of a low-melting isomer of 2,5-dimethyl-4-piperidol (I), which had a m.p. of 96.5-97° after recrystallization from benzene and acetone.

3.228 mg substance: 7.677 mg CO_2; 3.410 mg H_2O. 3.210 mg substance: 7.657 mg CO_2; 3.410 mg H_2O. Found %: C 64.90, 65.10; H 11.82, 11.85. $C_7H_{15}ON$. Calculated %: C 65.07; H 11.70.

The picrate of the low-melting isomer of 2,5-dimethyl-4-piperidol settled out, after part of the alcohol had been driven off, from a mixture of the base and a saturated alcoholic solution of picric acid. Yellow crystals, m.p. 176-177° (from alcohol).

The hydrochloride of 2,5-dimethyl-4-piperidol was prepared by reacting a solution of the base in absolute alcohol with anhydrous hydrogen chloride. Driving off the solvent and recrystallizing twice from alcohol yielded large crystals with a m.p. of 218-219°.

2) A solution of 12.6 g of 2,5-dimethyl-4-piperidone (b.p. 67.5° at 7 mm; n_D^{18} 1.4660) in 15 ml of alcohol was heated with 0.3 g of Raney nickel catalyst in a 156-ml autoclave under a hydrogen pressure of 148 atm. Hydrogenation set in at 90-100° and was complete after 2 hours 15 minutes. The catalyst was filtered out, the alcohol driven off, and the product distilled in vacuo. This yielded 11.5 g of a partially crystallized mixture of isomers of 2,5-dimethyl-4-piperidol, with a b.p. of 86-90° at 6 mm. The crystals were pressed out on a glass filter, washed with a small quantity of acetone, and recrystallized from acetone. This yielded 2.5 g of the high-melting 2,5-dimethyl-4-piperidol (II) as light, lustrous lamellae with a m.p. of 138°.

3.474 mg substance:)) 8.220 mg CO_2; 3.675 mg H_2O. 3.310 mg substance: 7.850 mg CO_2; 3.310 mg H_2O. Found %: C 64.67, 64.72; H 11.83, 11.86. $C_7H_{15}ON$. Calculated %: C 65.07; H 11.70.

The picrate of the high-melting isomer of 2,5-dimethyl-4-piperidol was produced by mixing alcoholic solutions of the base and of picric acid and driving off part of the solvent. M.p. 177-178° (from alcohol). The mixed melting point with the picrate of the low-melting isomer of 2,5-dimethyl-4-piperidol described above was 144-147°.

The hydrochloride of the high-melting isomer of 2,5-dimethyl-4-piperidol was prepared by reacting a solution of the base in absolute alcohol with anhydrous hydrogen chloride. Large crystals crystallized out of the solution by the following day; they were filtered out and washed with a small quantity of alcohol. M.p. 208-210°. Crystals in the shape of thin lamellae were secured from the filtrate after anhydrous ether had been added to it. Their m.p. was likewise 208-210° after washing on the filter and drying.

1,2,5-Trimethyl-4-piperidol. 1) 14.1 g of 1,2,5-trimethyl-4-piperidol (b.p. 64-65° at 8.5 mm; n_D^{11} 1.4590) was dissolved in 350 ml of absolute alcohol, and 35 g of metallic sodium was added in small pieces to the alcoholic solution. The alcoholate solution was then diluted with 100 ml of water and neutralized with 165 ml of concentrated hydrochloric acid. The sodium chloride was filtered out of the neutralized solution, the alcohol was driven off, and the remaining solution was evaporated in a porcelain dish on a water bath to a volume of some 75 ml. The action of a solid alkali caused a layer of an amino alcohol to separate; this layer was repeatedly extracted with ether, dried with alkali, and fractionated in vacuo. This yielded 9 g of a mixture of isomeric 1,2,5-trimethyl-4-piperidols (b.p. 73-82° at 6 mm; n_D^{21} 1.4720), from which we secured 4.1 g of 1,2,5-trimethyl-4-hydroxypiperidine (III) with a b.p. 80-81° at 5 mm; n_D^{20} 1.4738; d_4^{20} 0.9522; MR 42.55; calculated 42.41.

3.790 mg substance:) 0.326 ml N_2 (21° at 730 mm). 4.530 mg substance: 0.385 ml N_2 (20° at 738 mm). Found %: N 9.59, 9.61. $C_8H_{17}ON$. Calculated %: N 9.78.

The picrate was prepared by mixing together the base and an alcoholic solution of picric acid. After the solvent had been driven off, it took three weeks for the thick, dark-red mass to crystallize. The picrate had a m.p. of 138-139° (yellow crystals) after the crystalline mass had been washed with ether and recrystallized three times from alcohol.

The hydrochloride was prepared by passing a current of anhydrous hydrogen chloride through an alcoholic solution of the base. Driving off the solvent left behind an oily product. Precipitation with ether from the alcoholic solution threw down crystals together with an oily product. Heating in acetone with a small quantity of alcohol yielded crystals (m.p. 176-182°), which settled out again together with an oil when they were dissolved in alcohol and precipitated with ether. Crystals of 1,2,5-trimethyl-4-piperidol, with a m.p. of 192-194°, were isolated by fractional precipitation with ether from an alcoholic solution.

2) 13.5 g of 1,2,5-trimethyl-4-piperidone (b.p. 63-64° at 7 mm; n_D^{21} 1.4578) were hydrogenated in 30 ml of alcohol with a platinum catalyst. At the start hydrogen is absorbed rapidly, but within an hour, after 500 ml had been absorbed, absorption slowed down, taking 36 hours to be completed. A total of 2.4 liters of hydrogen was absorbed. Fractionation of the hydrogenation product in vacuo yielded 11 g of a mixture of isomeric amino alcohols (b.p. 81-88° at 7 mm), from which double fractionation yielded 8.5 g of 1,2,5-trimethyl-4-piperidol (IV) as a colorless, viscous liquid with the odor of an amine; b.p. 96-96.5° at 10 mm; 87-88° at 7 mm; n_D^{20} 1.4750; d_4^{20} 0.9549; MR 42.22; calculated 42.41.

7.67 mg substance; 18.83 mg CO_2; 8.32 mg H_2O. 8.34 mg substance: 20.42 mg CO_2; 9.13 mg H_2O. Found %: C 67.00, 66.81; H 12.14, 12.25. $C_8H_{17}ON$. Calculated %: C 67.09; H 11.96.

The picrate of 1,2,5-trimethyl-4-piperidol was prepared by mixing the base with an alcoholic solution of picric acid. Driving off the solvent yielded the crystals of the picrate, which had a m.p. of 116-118° after recrystallization from alcohol.

1,2,3,6-Tetramethyl-4-piperidol. 15.5 g of 1,2,3,6-tetramethyl-4-piperidone (b.p. 71° at 6.5 mm; n_D^{19} 1.4670) was dissolved in 350 ml of absolute alcohol, and 35 g of metallic sodium was added in small pieces to the alcoholic solution. After all the sodium had been added, the alcoholate solution was diluted with 150 ml of water and neutralized by gradually adding 165 ml of concentrated hydrochloric acid. The precipitated sodium chloride was filtered out, the alcohol was driven off from the filtrate, and the latter was evaporated to a volume of 70-90 ml in a porcelain dish on a water bath. The free base was isolated by the action of a solid alkali, extracted with ether, and dried in vacuo. This yielded 9.5 g of 1,2,3,6-tetramethyl-4-piperidol as a viscous, colorless liquid with the faint odor of an amine; b.p. 100-102° at 7 mm; n_D^{20} 1.4830; d_4^{20} 0.9626; MR 46.65; calculated 47.03.

Four days later crystals appeared on the bottom of the flask containing the reaction product, their quantity increasing slightly after the mixture had been chilled and rubbed with a rod. The crystals were filtered out on a dense glass filter and washed on the filter with a small quantity of acetone. This yielded about 0.1 g of a crystalline isomer of 1,2,3,6-tetramethyl-4-piperidol (V), with a m.p. of 77-79°, which was soluble in water, alcohol, ether, petroleum ether, acetone, carbon tetrachloride, benzene, and ligroin.

5.310 mg substance: 13.325 mg CO_2; 5.745 mg H_2O. 4.160 mg substance: 10.400 mg CO_2; 4.480 mg H_2O. Found %: C 68.48, 68.22; H 12.10, 12.05. $C_9H_{19}ON$. Calculated %: C 68.74; H 12.18.

Picrate. When alcoholic solutions of the base and of picric acid were mixed together, crystals of the picrate settled out after part of the solvent had been driven off. M.p. 181-182° (from alcohol.)

Picrolonate. When an alcoholic solution of crystalline 1,2,3,6-tetramethyl-4-piperidol was mixed with a hot solution of picrolonic acid and the solution cooled, the crystals of the picrolonate settled out; m.p. 213-214° (from alcohol). After the crystalline 1,2,3,6-tetramethyl-4-piperidol (7 g) had been filtered out, the filtrate was dissolved in a small quantity of alcohol and mixed with a hot solution of 13.6 g of picric acid in 120 ml of alcohol. Fractional crystallization of the resultant picrates yielded 3.5 g of the picrate described above, with a m.p. of 181-182°, from which we secured the crystalline 1,2,3,6-tetramethyl-4-piperidol, with a m.p. of 77-79°. We also secured 8.5 g of a picrate with a m.p. of 104-106° (from alcohol); decomposing this picrate with a 50% aqueous solution of potash, first in the cold and then by heating on a water bath, yielded 2.5 g of the liquid isomer of 1,2,3,6-tetramethyl-4-piperidol (VI) with a b.p. of 92-93° at 4 mm; n_D^{20} 1.4830.

4.420 mg substance: 11.080 mg CO_2; 4.830 mg H_2O. 4.108 mg substance: 10.300 mg CO_2; 4.470 mg H_2O. Found %: C 68.41, 68.42; H 12.23, 12.18. $C_9H_{19}ON$. Calculated %: C 68.74; H 12.18.

Picrolonate. When an alcoholic solution of the liquid isomer of 1,2,3,6-tetramethyl-4-piperidol was heated with a solution of picrolonic acid and then allowed to cool, the crystals of the picrolonate settled out; m.p. 202-204° (from alcohol.)

A mixture of the picrates of the isomeric 1,2,3,6-tetramethyl-4-piperidols also yielded about 0.4 g of the dipicrate of 1,2,3,6-tetramethyl-4-methylaminopiperidine with a m.p. of 232-233°, previously described [6] and only slightly soluble in alcohol, which was produced by reducing 1,2,3,6-tetramethyl-4-methylaminopiperidine, which was, in turn, produced by the action of an excess of monomethylamine upon 1,2,3,6-tetramethyl-4-piperidone during the course of the latter's synthesis. The mixed melting point of this dipicrate with the dipicrate of pure 1,2,3,6-tetramethyl-4-methylaminopiperidine exhibited no depression.

2,5-Dimethyl-6-ethyl-4-piperidol (VII). 5 g of 2,5-dimethyl-6-ethyl-4-piperidone (b.p. 80-81° at 7 mm; n_D^{20} 1.4658) was dissolved in 140 ml of absolute alcohol, and 13 g of metallic sodium, in small pieces, was gradually added to the solution. The product was diluted with 50 ml of water and neutralized by adding 60 ml of concentrated hydrochloric acid. The precipitated sodium chloride was filtered out, and the filtrate evaporated to a volume of 35-40 ml in a porcelain dish on a water bath. Sodium hydroxide was added to the aqueous solution, the precipitated base being extracted with ether, dried with fused alkali, and fractionated in vacuo. This yielded 3.8 g of a mixture of the isomeric 2,5-dimethyl-6-ethyl-4-piperidols, with a b.p. of 89-94° at 5 mm; n_D^{20} 1.4770. The product crystallized in part two days later. The crystals were pressed out on a glass filter, washed with acetone, and recrystallized from benzene. Colorless needles with a m.p. of 136-137°.

3.234 mg substance: 8.140 mg CO_2; 3.600 mg H_2O. 5.456 mg substance: 13.769 mg CO_2; 6.125 mg H_2O. Found %: C 68.69, 68.87; H 12.46, 12.56. $C_9H_{19}ON$. Calculated %: C 68.74; H 12.10.

The picrate was prepared by dissolving 0.1 g of the base (m.p. 136-137°) in 5-6 ml of a saturated alcoholic solution of picric acid. One hour later crystals of the picrate began to form. M.p. 226-228° after recrystallization from alcohol (darkens at 215-220°).

2-Methyl-6-ethyl-5-propyl-4-piperidol (VIII). 5.2 g of 2-methyl-6-ethyl-5-propyl-4-piperidone (b.p. 81-82° at 3 mm; n_D^{20} 1.4644) was dissolved in 130 ml of absolute alcohol, and 13 g of metallic sodium was added in small pieces. The product was distilled with 50 ml of water and neutralized by adding 60 ml of concentrated hydrochloric acid. The sodium chloride was filtered out of the solution, which was evaporated in a porcelain dish on a water bath to a volume of 50 ml. The free base was isolated from the aqueous solution by adding a solid alkali and extracting with ether. After the ether had been driven off the residue crystallized partially. When we endeavored to crystallize from benzene and ligroin, we secured a few crystals saturated with oil.

When the reaction product was heated with water to 60-70°, solid crystals settled out; they were collected and pressed out on a porous porcelain plate to remove the traces of oil. A waxy mass was scraped off the plate, which was recrystallized from benzene, yielding 2-methyl-6-ethyl-5-propyl-4-piperidol (VIII), with a m.p. of 123°.

3.351 mg substance: 8.640 mg CO_2; 3.730 mg H_2O. 3.291 mg substance: 8.490 mg CO_2; 3.690 mg H_2O. Found %: C 70.36, 70.40; H 12.45, 12.55. $C_{11}H_{23}ON$. Calculated %: C 70.76; H 12.51.

The picrate was prepared by dissolving 0.1 g of the base (m.p. 123°) in 5 ml of a saturated alcoholic solution of picric acid. One hour later the crystals began to settle out. M.p. 220° after recrystallization from alcohol.

2-Methyl-4-hydroxydecahydroquinoline. 11 g of 2-methyl-4-ketodecahydroquinoline (b.p. 107° at 3 mm; $n_D^{\text{[illegible]}}$ 1.4990) was dissolved in 400 ml of alcohol and stirred while 30 g of metallic sodium, cut into small bits, was added to the solution. The product was neutralized by adding 140 ml of concentrated hydrochloric acid, the sodium chloride being filtered out of the alcoholic solution and washed on the filter with hot alcohol. The filtrate was evaporated to a volume of 60-70 ml and decomposed by the action of a solid alkali. The separating layer of the base was extracted with ether. When the ether was driven off from the ether solution that had been dried with potash, crystals impregnated with a thick oil settled out. Repeated boiling with ligroin yielded about 7 g of a mixture of crystals, subsequent crystallization of which from acetone yielded the low-melting isomer of 2-methyl-4-hydroxydecahydroquinoline (IX), with a m.p. of 111-113° (from acetone), which was readily soluble in acetone.

4.280 mg substance: 11.119 mg CO_2; 4.374 mg H_2O. 5.368 mg substance: 13.985 mg CO_2; 5.628 mg H_2O. Found %: C 70.90, 71.08; H 11.60, 11.70. $C_{10}H_{19}ON$. Calculated %: C 70.95; H 11.32.

We also secured the high-melting isomer of 2-methyl-4-hydroxydecahydroquinoline (X), with a m.p. of 185-186°, which was less soluble in acetone.

5 720 mg substance: 14.827 mg CO_2; 5.678 mg H_2O. 3.225 mg substance: 8.348 mg CO_2; 3.280 mg H_2O. Found %: C 70.74, 70.64; H 11.10, 11.30. $C_{10}H_{19}ON$. Calculated %: C 70.95; H 11.32.

SUMMARY

Reducing substitution derivatives of the γ-piperidones with metallic sodium in alcohol or catalytically hydrogenating them above a nickel or platinum catalyst yields the corresponding alcohols of the piperidine series, usually as a mixture of two or more stereoisomers. The relative proportions of these isomers may vary widely, depending upon the reaction conditions. In the case of 2,5-dimethyl-4-piperidone, reduction with metallic sodium in alcohol results in the formation of individual 2,5-dimethyl-4-piperidol with a m.p. of 96-97°, whereas catalytic hydrogenation with an Ni catalyst yields a mixture of stereoisomers, the 2,5-dimethyl-4-piperidol with a m.p. of 138° predominating. Reducing the carbonyl group in γ-piperidones that have three or more substituents attached to the piperidine ring yields complex mixtures of stereoisomers of the γ-piperidols.

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[5] I. N. Nazarov and V. A. Rudenko. Bull. USSR Acad. Sci., Div. Chem. Sci. 610 (1948).

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Received June 2, 1950

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DERIVATIVES OF ACETYLENE

139. HETEROCYCLIC COMPOUNDS.

XV. Synthesis of Thiopyran Acids by Condensing Tetrahydro-γ-Thiopyrones with Ethyl Cyanacetate and Bromoacetate

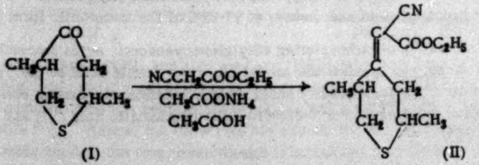
I. N. Nazarov and A. I. Kuznetsova

We recently published a new and simple method of synthesizing various tetrahydro-γ-thiopyrones [1], which can be used as initial products in the search for and synthesis of new physiologically active and medicinal substances.

We know from the literature that the sulfone corresponding to the amide of 4-benzyltetrahydro-1-thiopyran-4-carboxylic acid is an anesthetic [2].

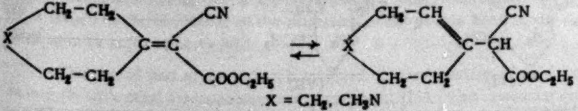
In synthesizing thiopyran acids we investigated the condensation of 2,5-dimethyl-tetrahydro-1-thiopyran-4-one (I) with ethyl cyanacetate and bromoacetate. As in the simple aliphatic ketones [3] and in 1-methyl-4-piperidone [4], we were unable to condense the thiopyrone (I) with malonic ester in the presence of ammonium acetate or piperidine and acetic acid. Nor was this condensation successful when sodium ethylate and sodium iodide were employed, though a yield of 25-30% was secured when cyclohexanone was treated under these same conditions [5].

When we condensed the thiopyrone (I) with ethyl cyanacetate in a benzene solution containing ammonium acetate and acetic acid, continuously removing the water produced from the reaction zone [4], we obtained the ethyl ester of 2,5-dimethyltetrahydro-4-thiopyrylidenecyanacetic acid (II), the yield being 75%:



(I) (II)

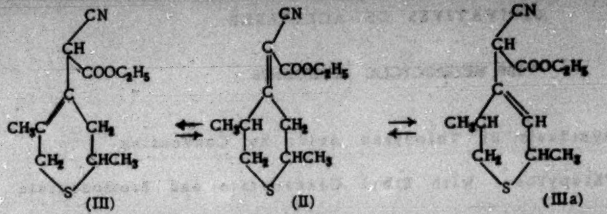
The problem of the structure of cyclohexylidine cyanacetate, which is an analog of the compound (II) we have synthesized, has been discussed in the literature for a long time [6]. The problem of the structure of the condensation products of γ-piperidones and ethyl cyanacetate has been recently resolved. It has been shown that compounds of this sort can react in two tautomeric forms:



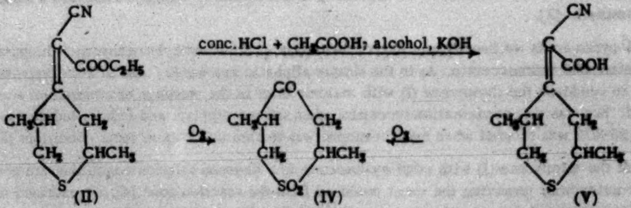
$X = CH_2,\ CH_3N$

These compounds possess a dual reactivity. On the one hand, they can react like compounds possessing a double bond conjugated with a carbonyl group, while on the other, they enter into reactions that are characteristic of an active hydrogen atom in the ethyl cyanacetate itself.

Apparently, the ethyl thiopyrylidenecyanacetate (II) we have synthesized can likewise react in two tautomeric forms (II-III) or (II-IIIa):

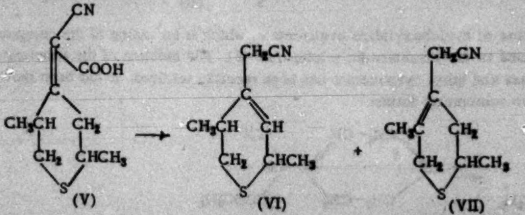

CN
CH
COOC₂H₅
CH₃C
CH₂
CH₂
CHCH₃
S
(III)
CN
C
COOC₂H₅
CH₃CH
CH₂
CH₂
CHCH₃
S
(II)
CN
CH
COOC₂H₅
CH₃CH
CH
CH₂
CHCH₃
S
(IIIa)

Ozonating the ethyl thiopyrylidenecyanacetate (II) yielded the sulfone (IV) we have described previously [1]. The nitrile group of the compound (II) is highly stable, being saponified neither under alkaline or acid conditions. The principal result of saponifying the ethyl thiopyrylidenecyanacetate (II) with an alcoholic solution of potassium hydroxide is the cleavage of the molecule at the double bond, yielding the thiopyrone (I) and a small quantity of 2,5-dimethyltetrahydro-4-thiopyrylidenecyanacetic acid (V), the m.p. of which is 162-163°. Ethyl thiopyrylidenecyanacetate (II) is unaffected by dilute mineral acids. When it is heated in an acetic acid solution with concentrated sulfuric acid, a high yield of thiopyrylidenecyanacetic acid (V) is produced, ozonation of which yields the cyclic sulfone (IV):


CN
C
COOC₂H₅
CH₃CH
CH₂
CH₂
CHCH₃
S
(II)
conc.HCl + CH₃COOH; alcohol, KOH
O₃
CO
CH₃CH
CH₂
CH₂
CHCH₃
SO₂
(IV)
O₃
CN
C
COOH
CH₃CH
CH₂
CH₂
CHCH₃
S
(V)

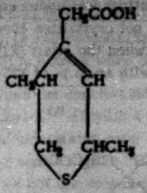
The action of methylmagnesium iodide on ethyl thiopyrylidenecyanacetate (II) evolved methane, which is evidence of the presence of a mobile hydrogen atom and, hence, of 21-22% of the tautomeric form (III) or (IIIa).

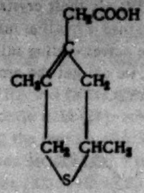
As several authors have pointed out [7], decarboxylating alkylidenecyanacetic acids proceeds smoothly when these acids are heated to 160-180° in vacuo, and involves the migration of the double bond to the γ-position. Thiopyrylidenecyanacetic acid (V) is also decarboxylated readily under these conditions, the double bond shifting to the ring, yielding a mixture of the nitriles of 2,5-dimethyl-$\Delta^{3,4}$-dihydro-4-thiopyranacetic acid (VI) and 2,5-dimethyl-$\Delta^{4,5}$-dihydro-4-thiopyranacetic acid (VII):

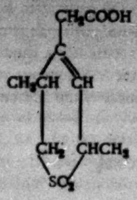

CN
C
COOH
CH₃CH
CH₂
CH₂
CHCH₃
S
(V)
CH₂CN
C
CH₃CH
CH
CH₂
CHCH₃
S
(VI)
+
CH₂CN
C
CH₃C
CH₂
CH₂
CHCH₃
S
(VII)

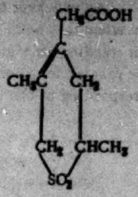
The β,γ-position of the double bond in these compounds is established by the absence of exaltation of the molecular refraction, and by the complete absence of the cyclic sulfone (IV) in the ozonation products of these nitriles.

No ammonia was evolved nor was the thiopyrone (I) formed when a mixture of the nitriles (VI) and (VII) was boiled with an alcoholic solution of potassium hydroxide, so that the nitrile group was not saponified nor did cleavage occur at the double bond thereby. When the nitriles (VI) and (VII) were heated to 70-80° with concentrated hydrochloric acid in acetic acid, we secured a mixture of acid amides, which were not isolated in the pure state and were then saponified by boiling them with a solution of potassium hydroxide in isoamyl alcohol. This yielded a mixture of the respective unsaturaturated acids (VIII) and (IX) as a viscous liquid, from which we isolated a small quantity of the crystals of individual 2,5-dimethyl-$\Delta^{3,4}$-dihydro-4-thiopyranacetic acid (VIII) with an m.p. of 94-95°.


(VIII) m.p. 94-95°

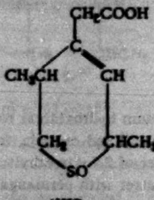

(IX) m.p. 88-89°

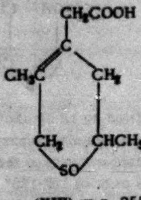

(X) m.p. 185°


(XI) m.p. 146-147°

Oxidation of the latter with perhydrol in glacial acetic acid yielded the corresponding sulfone (X) with an m.p. of 185°.

We succeeded in separating the liquid mixture of the unsaturated acids (VIII) and (IX) by using the crystalline sulfones (X) and (XI). Oxidation of the liquid mixture of the acids (VIII) and (IX) with perhydrol at room temperature yielded the sulfoxide (XIII), with an m.p. of 255-256°, the second sulfoxide (XII) not being secured in this procedure. Boiling the sulfoxide (XIII) with perhydrol in glacial acetic acid yielded the sulfone (XI) with an m.p. of 146-147°. The residue left after the sulfoxide had been filtered out also yielded the two sulfones (X) and (XI), the m.p. of which were 185° and 146-147°.

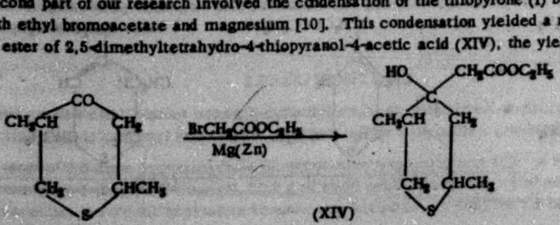

(XII)


(XIII) m.p. 255-256°

The unsaturated acids (VIII) and (IX) we have synthesized, and their sulfones (X) and (XI), do not add ozone at the double bond, while oxidizing them with permanganate results in far-reaching destruction of the molecule. The oxidation products contain absolutely no sulfone (IV), so that these compounds do not contain a semicyclic double bond. Hence, the only possible explanation for the isomerism of these compounds is the position of the double bond in the ring, even though this position has not been definitely established, because of the difficulty of identifying the oxidation products.

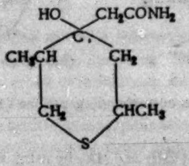
When we consider the transformations described above, beginning with the synthesis of ethyl thiopyrylidenecyanacetate (II) and ending with the formation of the dihydrothiopyranacetic acids (VIII) and (IX), we may regard it as certain that the shift of the double bond from the alpha-beta position to the beta, gamma position took place during the decarboxylation of thiopyrylidenecyanacetic acid (V). There are references in the literature to the feasibility of the migration of the double bond in alpha, beta unsaturated acids when acted upon by acids or bases [8].

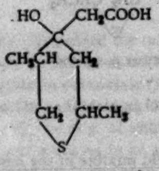
The second part of our research involved the condensation of the thiopyrone (I) by the Reformatsky method [9] with ethyl bromoacetate and magnesium [10]. This condensation yielded a mixture of geometric isomers of the ester of 2,5-dimethyltetrahydro-4-thiopyranol-4-acetic acid (XIV), the yield being 53%:

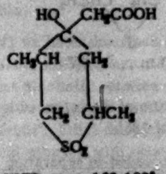

(I) (XIV)

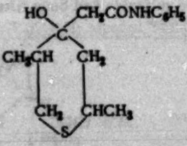
The reaction hardly takes place at all when zinc is substituted for magnesium, only an insignificant percentage of the ester (XIV) being produced.

An endeavor to separate the geometric isomers (XIV) via their crystalline derivatives was unsuccessful. When they were oxidized with permanganate, we obtained a hyaline mass that did not crystallize even after standing for a long time, apparently a mixture of the corresponding sulfones. But when the esters (XIV) were reacted for a long time with 30% aqueous ammonia, we did get the amide (XV), with an m.p. of 123-124°, corresponding to one of the isomers of the hydroxy acid (XVI).


(XV) m.p. 123-124°


(XVI) m.p. 132-133°
m.p. 116-117°


(XVII) m.p. 192-193°
m.p. 178-179°


(XVIII) m.p. 136-137°

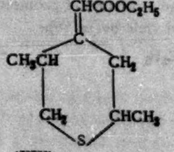
The ester (XIV) is readily saponified by an alcoholic solution of potassium hydroxide at room temperature. This yielded a mixture of the stereoisomeric hydroxy acids (XVI) as a liquid and crystals, from which all we were able to secure was a negligible quantity of the high-melting isomer of 2,5-dimethyltetrahydro-4-thiopyranol-4-acetic acid (XVI), with an m.p. of 132-133°. Oxidation of the latter with permanganate yielded the corresponding sulfone (XVII), with an m.p. of 192-193°, while boiling with aniline yielded the anilide (XVIII).

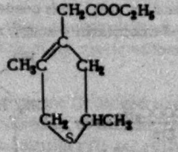
The esters of the hydroxy acids (XVI) were dehydrated with potassium bisulfate.

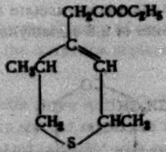
We know from the literature [11] that when the similar cyclohexane hydroxy acids are dehydrated with various catalysts, the resultant products are always acids that have a semicyclic double bond and acids that have a double bond in the ring, as was the case in the thiopyran series.

Apparently, the high-melting isomer of the hydroxy acid (XVI) described above can be dehydrated by potassium bisulfate under milder conditions (150-160°) than the other isomer. Careful dehydration of the mixture of stereoisomeric hydroxy esters (XIV), followed by fractionation and saponfication, yielded the low-melting isomer of 2,5-dimethyltetrahydro-4-thiopyranol-4-acetic acid (XVI), with an m.p. of 116-117°. Oxidizing this acid with an aqueous permanganate solution yielded the corresponding sulfone (XVII), with an m.p. of 178-179°.

When a mixture of the stereoisomeric hydroxy esters (XIV) is dehydrated with potassium bisulfate under more severe conditions (at 195-200°), the process goes to completion, yielded a mixture of the unsaturated esters (XIX) and (XX), which differ in the position of their double bonds.


(XIX)

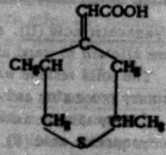

(XX)


(XXI)

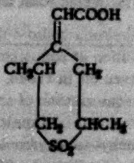
The unsaturated ester (XIX) with a semicyclic double bond largely predominates in the dehydration products. We assign the structure (XX) to the other unsaturated ester because dehydration of compounds of the (XIV) type involves solely the branched carbon atom that possesses a methyl group, as has been shown for the pyran and cyclohexane series [12]. That is why we regard it highly unlikely that the unsaturated ester (XXI) is formed when the hydroxy ester (XIV) is dehydrated.

When the unsaturated esters (XVIII) and (XIX) were fractionated, we obtained a small quantity of 2,5-dimethyl-Δ^{4-5}-dihydro-4-thiopyranacetic acid (IX), with an m.p. of 88-89°, produced by the saponfication of the unsaturated ester (XX) during the proces of dehydration, i.e., by the action of the potassium bisulfate and water. When the thiopyranacetic acid (IX) was oxidized with perhydrol in a glacial acetic acid solution, we got the corresponding sulfone (XI), with an m.p. of 146-147°, which exhibited no depression of the melting point when mixed with the sample described above, produce by condensation with ethyl cyanacetate.

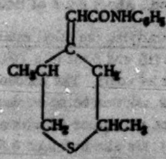
The unsaturated esters (XIX) and (XX) of the thiopyran series are saponified at different rates, the esters with a semicyclic double bond being harder to saponify, it seems. When a mixture of the unsaturated esters (XIX) and (XX) was reacted for half an hour with an alcoholic solution of potassium hydroxide, part of an unsaturated ester did not react. Subsequent saponification of this residue yielded 2,5-dimethyltetrahydro-4-thiopyrylideneacetic acid (XXII), with an m.p. of 111-112°.



(XXII) m.p. 111-112°



(XXIII) m.p. 198°



(XXI m.p. 153-154°

Oxidation of (XXII) with perhydrol in acetic acid yielded the corresponding sulfone (XXIII), with an m.p. of 198°, while boiling it with aniline yielded the anilide (XXIV), with an m.p. of 153-154°.

Ozonating the unsaturated acid (XXII) yielded the sulfone (IV), thus proving that this compound has a semicyclic double bond.

In an effort to separate the liquid mixture of the unsaturated acids (XXII) and (IX), we tried to secure their crystalline derivatives. But when we oxidized the mixture with perhydrol in glacial acetic acid, only a single sulfone (XXIII) was isolated from the sulfone mixture, while boiling the acid mixture with aniline yielded solely a high percentage (about 50%) of the anilide (XXIV).

The hydroxy acids (XVI) themselves can be dehydrated by potassium bisulfate at 200-220°. Boiling the resultant mixture of unsaturated acids with aniline likewise yielded nothing but the aniline (XXIV).

There is thus no doubt that the principal product of the dehydration of the hydroxy esters of the thiopyran series (XIV) is the unsaturated ester (XIX) with a semicyclic double bond, saponification of which yields the acid (XXII). A smaller amount of the other ester (XX), with a doulbe bond in the ring, is produced when the hydroxy esters (XIV) are dehydrated.

All the unsaturated thiopyran acids and esters, as well as the corresponding sulfones, described in this paper are not hydrogenated by hydrogen with palladium and platinum catalysts, even at 100° in solutions of alcohol dioxane, and acetic acid.

EXPERIMENTAL

We used as the initial product trans-2,5-dimethyltetrahydro-1-thiopyran-4-one (I) (m.p. 70-71°), produced by reacting allyl isopropenyl ketone with hydrogen sulfide as described previously [1].

Ethyl ester of 2,5-dimethyltetrahydro-4-thiopyrylidenecyanacetic acid (II). A mixture of 43 g of 2,5-dimethyltetrahydro-1-thiopyran-4-one (I), 30.8 g of ethyl cyanacetate, 3.3 ml of glacial acetic acid, 2.4 g of ammonium acetate, and 30 ml of absolute benzene was boiled at 130-160° for 1.5 hours in a flask connected to a reflux condenser via a water trap [4]. The water collecting in the water trap was removed at intervals (a total of 6 ml was collected). The reaction liquid was washed three times with 10-ml portions of water, the aqueous layer being extracted with benzene, and the benzene solutions combined together and dried with magnesium sulfate. Vacuum fractionation yielded 12 g of the unreacted thiopyrone (I) and 49 g of the ethyl ester of 2,5-dimethyltetrahydro-4-thiopyrylidenecyanacetic acid (II); b.p./6 mm 153-160° n_D^{21} 1.5250. (The yield was 75.2% of the theoretical.)

The synthesized ester was colorless liquid with an unpleasant odor:

B.p./5 mm 154-155°; n_D^{20} 1.5255; d_4^{20} 1.1072; MR 66.29; calculated 64.39.

6.462 mg substance: 14.231 mg CO_2; 4.245 mg H_2O; 2.622 mg SO_4. Found %: C 60.10; H 7.35; S 13.54. $C_{12}H_{17}O_2NS$. Calculated %: C 60.22; H 7.15; S 13.39.

Ozonation of the ethyl ester of 2,5-dimethyltetrahydro-4-thiopyrylidenecyanacetic acid (II). Ozonized oxygen (6% ozone concentration) was passed through a solution of 0.7 g of the ester (I) in 50 ml of chloroform for 3 hours. The resultant ozonide was decomposed by heating the chloroform solution with 20 ml of water to 60° for 2 hours. The water and the chloroform were driven off at a low vacuum. The residue — a thick oil — was dissolved in benzene, washed with an aqueous soda solution, and dried with magnesium sulfate. Driving off the benzene yielded 0.2 g of the sulfone (IV), m.p. 138°. Its mixed melting point with a known sample exhibited no depression. About 0.2 g of liquid acids was recovered from the aqueous solution in the usual manner.

Saponifying the ethyl ester of 2,5-dimethyltetrathydro-4-thiopyrylidenecyanacetic acid (II). a) 2 grams of the ester (II) and 6 ml of a 10% alcoholic solution of potassium hydroxide were allowed to stand at room temperature for 24 hours. The alcohol was then driven off in vacuo, using no heat. The solid residue was dissolved in ether, the solution being washed with an aqueous solution of soda. The customary processing and drying yielded 1 g of the thiopyrone (I) with an m.p. of 71°. (Its mixed melting point with a known sample exhibited no depression.) We also obtained 0.5 g of 2,5-dimethyl-tetrahydro-4-thiopyrylidenecyanacetic acid (V), with an m.p. of 162-163°, which exhibited no depression when mixed with the sample described below. Saponification of the ester (II) with a normal solution of potassium hydroxide or by boiling with a 5% solution of soda, yielded the same results.

b) 3.75 g of the ether (II), 10 ml of glacial acetic acid, and 20 ml of concentrated hydrochloric acid were heated together, with constant stirring, to 75-85° for 23 hours. The acetic acid was driven off in vacuo, and the residue was dissolved in ether and washed with a soda solution until its reaction was neutral. Evaporation of the soda solution, acidulation, and ether extraction of the acid products yielded 3.4 g of 2,5-dimethyltetrahydro-4-thiopyrylidenecyanacetic acid (V) as colorless needles with an m.p. of 162-163° (from benzene).

0.0942 g substance: 4.34 ml 0.1 N KOH. 5.139 mg substance: 10.747 mg CO_2; 2.938 mg H_2O; 2.373 mg SO_4. 5.438 mg substance: 11.362 mg CO_2; 3 070 mg H_2O; 2.460 mg SO_4. Found : M 214.23; %: C 57.07, 57.02; H 6.40, 6.32; S 15.42, 15.10. $C_{10}H_{13}O_2NS$. Calculated: M 211.26; %: C 56.85; H 6.20; S 15.14.

Ozonating 2,5-dimethyltetrahydro-4-thiopyrylidenecyanacetic acid (V). Ozonized oxygen (containing 6% ozone) was passed through a solution of 0.4 g of the acid (V) in 50 ml of chloroform for 6 hours. After the customary decomposition of the ozonide by heating with water, the water and the chloroform were driven off in vacuo, the product was dissolved in benzene and washed with a solution of soda, and the benzene solution was dried with magnesium sulfate. After the benzene had been driven off, the residue consisted of 0.15 g of the sulfone (IV), which had an m.p. of 137-138° after three recrystallizations and exhibited no depression of the mixed melting point with a known sample. We also obtained 0.1 g of acid products, which were not analyzed.

Action of methylmagnesium bromide upon the ethyl ester of 2,5-dimethyltetrahydro-4-thiopyrylidenecyanacetic acid (II). The active hydrogen in the ester (II) was determined by the Chugayev-Tserevitinov method in a solution of dibutyl ether.

0.3443 g substance: 8.1 ml methane (19°, 740 mm). 0.4727 g substance: 10.3 ml methane (18°, 745 mm). Found %: active H 0.0961, 0.0900. From formula (III) or (IIIa) calculated %: active H 0.4210.

Decarboxylating 2,5-dimethyltetrahydro-4-thiopyrylidenecyanacetic acid (V). 49 g of the ester (II), 150 ml of glacial acetic acid, and 300 ml of concentrated sulfuric acid were heated together to 70-80°, with constant stirring, on a water bath for 23 hours. The acetic acid and the water were dirven off at a low vacuum.

The residue was neutralized with soda, the neutral products being extracted with ether and dried with magnesium sulfate. We recovered 3.3 g of the ester (II) (b.p. 150-175° at 9 mm; n_D^{21} 1.5220) plus 2 g of the thiopyrone (I).

After the ether had been driven off from the acid reaction products, secured from the soda solution in the usual manner, we obtained about 30 g of the acid (V) as a thick oil and crystals, which were decarboxylated by heating them in vacuo to 170-175°, without further purification. The vacuum was gradually raised from 30 mm to 15 mm, causing distillation to start and finally yielding 16.6 g of a mixture of the nitriles of 2,5-dimethyldihydro-4-thiopyranacetic acid (VI) and (VII) as a colorless liquid with a b.p. of 150-160° at 15 mm; n_D^{20} 1.5252.

We collected a fraction with a b.p. of 114-115° at 2 mm; n_D^{20} 1.5262; d_4^{20} 1.0543; MR 48.71; calculated 48.88, for analysis.

5.717 mg substance: 13.555 mg CO_2; 3.915 mg H_2O; 3.245 mg SO_4. 5.010 mg substance: 2.885 mg SO_4. Found %: C 64.70; H 7.66; S 18.95, 19.20. $C_9H_{13}NS$. Calculated % C 64.63; H 7.83; S 19.17.

Ozonating the nitriles of 2,5-dimethyldihydro-4-thiopyranacetic acid (VI) and (VII). Ozonized oxygen (6% ozone) was passed through a solution of 1.4 g of the mixture of the nitriles (VI) and (VII) described above for 2 hours. The resultant ozonide was decomposed by heating it to 60° with water. The chloroform and the water were then driven off in vacuo. The residue, an oil, was dissolved in benzene and washed with a solution of soda. Drying and driving off the benzene yielded an oily residue totaling about 0.2 g, which crystallized after dilution with ether and rubbing with a rod. The crystals had an m.p. of 165-170° after recrystallization from alcohol; they were analyzed no further. We also obtained about 0.1 g of acid products. None of the cyclic sulfone (IV) was found in this test.

Saponifying the nitriles of 2,5-dimethyldihydro-4-thiopyranacetic acid (VI) and (VII). 17.6 grams of the mixture of the nitriles (VI) and VII), 32 ml of glacial acetic acid, and 80 ml of concentrated hydrochloric acid were heated for 23 hours, with constant stirring. The acetic acid and the water were driven off in vacuo, the residue being diluted with 20 ml of water and the liquid re-evaporated. Then this entire operation was repeated. The residue was diluted with water and neutralized with soda, the acid and neutral products being separated in the customary manner. After the ether had been driven off from the acid products, 1.9 g of an oil that could not be distilled with decomposing was left as a residue. In one of our experiments, the acid reaction products yielded 2,5-dimethyldihydro-4-thiopyranacetic acid (VIII), with an m.p. of 94-95°. Driving the ether out of the neutral products left behind a residue of 10.5 g of thick liquid, which was, apparently, a mixture of the amides of 2,5-dimethyldihydro-4-thiopyranacetic acids (VIII) and (IX), with a b.p. of 140-148° at 0.02 mm. The resulting product was not refined, being employed for subsequent saponification. 6.5 grams of this substance was refluxed for 5 hours with 20 ml of 10% potassium hydroxide in isoamyl alcohol. Ammonia was evolved. The acid and neutral products were separated in the customary manner.

Driving the ether out of the acid products yielded 4 g of unsaturated acids as a thick liquid, which crystallized in part upon standing. The crystals were filtered out, fivefold recrystallization from benzene yielding 0.5 g of pure 2,5-dimethyl-Δ^{3-4}-dihydro-4-thiopyranacetic acid (VIII), with an m.p. of 94-95°.

4.957 mg substance: 10.550 mg CO_2; 3.345 mg H_2O; 2.530 mg SO_4. 4.348 mg substance: 9.208 mg CO_2; 3.028 mg H_2O; 2.205 mg SO_4. Found %: C 58.01, 57.80; H 7.54, 7.79; S 17.02, 16.93. $C_9H_{14}O_2S$. Calculated %: C 58.03; H 7.57; S 17.21.

After the crystals had been filtered out, the mother liquor was distilled in vacuo. This yielded 3 g of a liquid mixture of the acids (VIII) and (IX) (b.p./3 mm 145-151°; $n_D^{18.5}$ 1.5245), which also crystallized in part upon standing. Driving the ether out of the neutral products yielded 2.85 g of a thick oil that was not analyzed.

Oxidizing the crystalline 2,5-dimethyldihydro-4-thiopyranacetic acid to a sulfone. a) 0.2 gram of the crystalline acid (VIII) (m.p. 94-95°), 26 ml of glacial acetic acid, and 0.3 g of 30% perhydrol were allowed to stand at room temperature for 72 hours. Then the acetic acid was driven off in vacuo, the bath temperature not exceeding 50°. The residue crystallized. This yielded 0.2 g of the sulfone (X), whose m.p. was 185° (from water).

4.450 mg substance: 8.123 mg CO_2; 2.672 mg H_2O; 1.935 mg SO_4. Found %: C 49.81; H 6.72; S 14.51. $C_9H_{14}O_4S$. Calculated %: C 49.52; H 6.46; S 14.69.

b) Ozonized oxygen (5% ozone) was passed through a solution of 0.15 g of the acid (m.p. 94-95°) in 30 ml of chloroform for one hour at the rate of 5 liters per hour. After 20 ml of water had been added, the mixture was heated for 2 hours. The solution was evaporated to dryness, yielding 0.1 g of crystals of the sulfone (X), which had an m.p. of 185° and exhibited no depression with the preceding sample.

When ozonized oxygen (6% ozone) was passed through a chloroform solution of the sulfone (m.p. 185°) for 10 hours, no ozone was added at the double bond, the recovered sulfone having the same m.p. of 185° and exhibiting no depression with the initial sample. Similarly, the ozone was not added at the double bond of the isomeric sulfone (XI), with an m.p. of 146-147°.

Oxidizing a mixture of the 2,5-dimethyldihydro-4-thiopyranacetic acids (VIII) and (IX). 4.5 g of the mixture of the unsaturated acids(VIII) and (IX) described above, produced by saponifying the nitriles (VI) and (VII), was dissolved in 565 ml of glacial acetic acid, and 6.75 ml of 30% perhydrol was added to the solution. Two hours later the acetic acid was driven off in vacuo, the bath temperature not exceeding 50°. The thick residue was diluted with ether, precipitating 1.4 g of crystals of the sulfoxide (XIII), whose m.p. was 255-256° after repeated recrystallization from alcohol.

2.682 mg substance: 5.188 mg CO_2; 1.692 mg H_2O; 1.300 mg SO_4. 1.900 mg substance: 3.675 mg CO_2. 1.208 mg H_2O; 0.930 mg SO_4. Found %; C 52.79; H 7.06, 7.11; S 16.18, 16.34. $C_9H_{14}O_3S$. Calculated %: C 53.44, H 6.98; S 15.85.

After the sulfoxide had been filtered out of the ether solution, the ether was driven off, leaving a residue of 3.4 g of a hyaline substance. When this residue was diluted with water and rubbed with a rod, crystals of the sulfone (X) with an m.p. of 185°, described above, settled out. The aqueous solution was evaporated and rediluted with water; rubbing with a rod again threw down the sulfone with an m.p. of 185°. This operation was repeated one more time. This yielded a total of 0.5 g of the sulfone with an m.p. of 185°, which exhibited no depression when mixed with the sample described above. The remaining acid was diluted with ether, after which rubbing with a rod threw down the crystals of the other sulfone (XI), with an m.p. of 146-147°, which was also produced by oxidizing the sulfoxide described above.

0.2 gram of the sulfoxide (XII) (m.p. 255-256°) dissolved in 5 ml of glacial acetic acid, was boiled for 4 hours with 0.15 ml of 30% perhydrol. The reaction product was diluted with water (2 ml) and evaporated to dryness. This yielded 0.2 g of the other isomer of the sulfone (XI), with an m.p. of 146-147° (from water).

5.580 mg substance: 10.072 mg CO_2; 3.320 mg H_2O; 2.465 mg SO_4. 5.617 mg substance: 10.160 mg CO_2; 3.237 mg H_2O; 2.420 mg SO_4. Found %: C 49.26, 49.36; H 6.66, 6.45; S 14.74, 14.36. $C_9H_{14}O_4S$. Calculated %: C 49.52; H 6.46; S 14.69.

Oxidizing the sulfones (X) and (XI) with permanganate. Since neither of the isomeric sulfones (X) and (XI) adds ozone at the double bond, they were both oxidized with permanganate.

a) 0.6 grams of permanganate was gradually added, with stirring, to a solution of 0.5 g of the sulfone (m.p. 185°) in 40 ml of acetone and 1.5 ml of 10% sulfuric acid. Oxidation was carried out at room temperature and was finished in 30 minutes. The solution was completely decolorized. The customary treatment recovered 0.2 g of the sulfone with an m.p. of 185°. (Its mixed melting point with the initial product exhibited no depression.) Moreover, we obtained a small quantity of liquid acid products.

b) 50 ml of a 2% aqueous permanganate solution was gradually added, with stirring to a solution of 0.8 g of the sulfone (XI) (m.p. 146-147°) in 50 ml of acetone and 2.2 ml of 10% sulfuric acid. After the solution had been completely decolorized, the product was processed in the usual manner. This recovered 0.2 g of the sulfone with an m.p. of 146-147° (its mixed melting point exhiting no depression) plus traces of acid products.

Ethyl ester of 2,5-dimethyltetrahydro-4-thiopyranol-4-acetic acid (XIV): 36 grams of 2,5-dimethyltetrahydro-1-thiopyran-4-one (I) and 42 g of ethyl bromoacetate were dissolved in 150 ml of absolute benzene. 25 ml of the solution and 6 g of magnesium were placed in a three-necked flask, fitted with a mechanical stirrer, a reflux condenser, a dropping funnel, and a thermometer. A crystal of iodine was added, and the solution was heated on a water bath. A vigorous reaction set in at 65°. The bath was removed, the process being controlled by gradually adding the rest of the solution. The reaction mass was refluxed for 4.5 hours on a water bath and left to stand overnight. The next day the flask was chilled with ice water as the product was hydrolyzed with 15% acetic acid (240 ml), extracted with ether, washed with a bicarbonate solution, and dried with magnesium sulfate. Fractionation in vacuo recovered 7.1 g of the unreacted thiopyrone (I) and yielded 23.0 g of the ethyl ester of 2,5-dimethyltetrahydro-4-thiopyranol-4-acetic acid (XIV) as a colorless liquid:

B.p./4 mm 134°; n_D^{20} 1.4941; d_4^{20} 1.0966; MR 61.69; calculated 61.95.
4.073 mg substance: 1.752 ml 0.02 N I_2. Found %: S 13.79. $C_{11}H_{20}O_3S$. Calculated %: S 13.79.

Oxidizing the thiopyranol (XIV) to a sulfone. 20 ml of a 4% aqueous solution of permanganate was added, with ice-water chilling to a solution of 1 g of the thiopyranol (XIV) in 10 ml of acetone and 3.8 ml of 10% sulfuric acid. The manganese dioxide was washed with hot water, and the product was thoroughly extracted with ether, dried with magnesium sulfate and distilled in vacuo. This yielded 0.5 g of the sulfone as a noncrystallizing hyaline mass, with a b.p. of 183-185° at 0.5 mm; n_D^{20} 1.4931.

3.635 mg substance: 6.770 mg CO_2; 2.550 mg H_2O; 1.390 mg SO_4. 4.620 mg substance: 8.585 mg CO_2; 3.155 mg H_2O; 1.780 mg SO_4. Found %: C 50.85, 50.71; H 7.49, 7.64; S 12.75, 12.86. $C_{11}H_{20}O_5S$. Calculated %: C 49.97; H 7.62; S 12.13.

Amide of 2,5-dimethyltetrahydro-4-thiopyranol-4-acetic acid (XV). 6 ml of a 30% aqueous solution of ammonia was added to 2 g of the ester (XIV). The liquid, which had become homogeneous after one month had elapsed, was extracted with ether. The ether solution was dried and the ether driven off, the residue yielding 1.2 g of a thick, syrupy liquid, which crystallized when rubbed with a rod. The crystals were filtered out and recrystallized from benzene. This yielded 0.2 g of the amide (XV), which had an m.p. of 123-124°.

3.403 mg substance: 0.824 ml 0.02 N $KH(IO_3)_2$. 3.019 mg substance: 0.745 ml 0.02 N $KH(IO_3)_2$. 4.310 mg substance: 8.400 mg CO_2; 3.327 mg H_2O; 2.020 mg SO_4. 3.960 mg substance: 7.740 mg CO_2. 3.028 mg H_2O. 1.850 mg SO_4. Found %: N 6.78, 6.91; C 53.19, 53.34; H 8.64, 8.55; S 15.65, 15.60. $C_9H_{17}O_2NS$. Calculated %: N 6.89; C 53.16; H 8.43; S 15.77.

The customary processing of the aqueous solution yielded 0.5 g of acid products that were not analyzed.

Saponifying the ethyl ester of 2,5-dimethyltetrahydro-4-thiopyranol-4-acetic acid (XIV). 1) 5 grams of the ester (XIV) was dissolved in 14 ml of a 10% alcoholic solution of potassium hydroxide. 48 hours later the alcohol was driven off in vacuo, and the residue was dissolved in water and extracted with ether to eliminate the neutral products. The aqueous solution was acidulated with 6 ml of 15% hydrochloric acid and extracted with ether. Drying the product and driving off the ether yielded a residue of 4 g of a mixture of the stereoisomeric hydroxy acids (XVI) as a viscous liquid, which crystallized in part by the next day. The crystals were filtered out and recrystallized repeatedly from benzene. This yielded about 1 g of 2,5-dimethyltetrahydro-4-thiopyranol-4-acetic acid (XVI) as colorless needles with an m.p. of 132.5-133.5°.

0.1238 g substance: 6.04 ml 0.1 N KOH. 5.835 mg substance: 11.390 mg CO_2; 4.190 mg H_2O; 2.775 mg SO_4. 4.315 mg substance: 8.410 mg CO_2; 3.110 mg H_2O; 2.045 mg SO_4. Found: M 204.08; %: C 53.27, 53.19; H 8.03, 8.06; S 15.88, 15.82. $C_9H_{16}O_3S$. Calculated: M 204.28; %: C 52.90; H 7.89; S 15.69.

After the solid acid had been filtered out, the mother liquor was distilled in vacuo. This yielded about 3 g of a mixture of the stereoisomeric acids (XIV) as a hyaline mass with a b.p. of 150-162° at 0.02 mm.

0.2488 g substance: 12.46 ml 0.1 N KOH. 6.740 mg substance: 13.100 mg CO_2; 4.800 mg H_2O. 5.150 mg substance: 10.020 mg CO_2; 3.660 mg H_2O; 2.410 mg SO_4. Found: M 204.31; %: C 53.04, 53.10; H 7.97, 7.95; S 15.62. $C_9H_{16}O_3S$. Calculated: M 204.28; %: C 52.90; H 7.89; S 15.69.

When these acids were diluted with petroleum ether, crystals settled out, their m.p. being 96-97° after the first recrystallization from benzene, the m.p. rising to 98-99°, 98-102°, and 125-133° after subsequent recrystallizations.

An attempt to separate the isomers of the hydroxy acids (XVI) by recrystallization from other solvents (chloroform, ether, and acetone) was also unsuccessful. Nor could we separate the isomers by means of chromatography.

Oxidizing 2,5-dimethyltetrahydro-4-thiopyranol-4-acetic acid to a sulfone. An alcoholic solution of 0.2251 g of the hydroxy acid (XVI) (m.p. 132-133°) was back-titrated with a 0.1N solution of potassium hydroxide.

The solution was evaporated, and the residue was dissolved in water and oxidized with 5 ml of a 4% aqueous solution of permanganate. The manganese dioxide was washed with hot water, and the aqueous solution evaporated and acidulated with 30% sulfuric acid. This yielded 0.2 g of the sulfone (XVII), which had an m.p. of 192-193° after recrystallization from water.

8.84 mg substance: 14.98 mg CO_2; 5.52 mg H_2O. 9.09 mg substance: 15.42 mg CO_2;5.69 mg H_2O. Found %: C 46.24, 46.29; H 6.69, 7.00. $C_9H_{16}O_5S$. Calculated %: C 45.75; H 6.83.

Anilide of 2,5-dimethyltetrahydro-4-thiopyranol-4-acetic acid (XVIII). 1.15 grams of the hydroxy acid (XVI) (m.p. 132-133°) was heated to 180° for 10 hours with 2 g of freshly distilled aniline. The product was diluted with water, extracted with ether, washed with a 10% solution of hydrochloric acid, and dried with magnesium sulfate. Driving off the ether yielded 0.85 g of the anilide (XVIII), which had an m.p. of 136-137° (from benzene).

5.670 mg substance: 0.264 ml N_2 (20°, 735 mm). 5.608 mg substance: 0.261 ml N_2 (21°, 735 mm). 5.210 mg substance: 12.318 mg CO_2; 3.562 mg H_2O; 1.830 mg SO_4. 5.798 mg substance: 13.700 mg CO_2; 3.920 mg H_2O; 1.980 mg SO_4. Found %: N 5.25, 5.23; C 64.52, 64.48; H 7.65, 7.56; S 11.72, 11.40. $C_{15}H_{21}O_2NS$. Calculated %: N 5.01; C 64.48; H 7.58; S 11.47.

Dehydrating the ethyl ester of 2,5-dimethyltetrahydro-4-thiopyranol-4-acetic acid (XIV). a) 11 g of the hydroxy ester (XIV) was dehydrated by heating it to 150-160° for 3.5 hours with 20 g of finely pulverized anhydrous potassium bisulfate. After the reaction mass had cooled, it was dissolved in water, the product being extracted with ether, dried with magnesium sulfate, and fractionated in vacuo.

Fraction 1: 132-137° at 7 mm; n_D^{22} 1.5010 − 1.05 g;
Fraction 2: 137-142° at 7 mm; n_D^{22} 1.5020 − 1.1 g;
Fraction 3: 142-145° at 7 mm; n_D^{22} 1.5018 − 3 g.

When we saponified Fraction 3 with a 10% alcoholic solution of potassium hydroxide, we got 2.4 g of acids, part of which crystallized. The crystals were filtered out and recrystallized from benzene. This yielded 0.3 g of the second isomer of 2,5-dimethyltetrahydro-4-thiopyranol-acetic acid (XVI), with an m.p. of 116-117°.

0.1327 g substance: 6.52 ml 0.1 N KOH. 4.570 mg substance: 8.900 mg CO_2; 3.368 mg H_2O: 2.120 mg SO_4. Found: M 203.46; %: C 53.15; H 8.24; S 15.49. $C_9H_{16}O_3S$. Calculated: M 204.28; %: C 52.90; H 7.89; S 15.69.

0.1327 gram of this isomer of the hydroxy acid (XVI) (m.p. 116-117°) was dissolved in alcohol and back-titrated with a 0.1N solution of potassium hydroxide. The solution was evaporated to dryness, and the salt of the acid dissolved in 10 ml of water and oxidized with 25 ml of a 5% aqueous solution of permanganate. The customary processing yielded 0.1 g of the second isomer of the sulfone (XVII), with an m.p. of 178-179° (from water).

4.985 mg substance: 8.375 mg CO_2; 3.040 mg H_2O. Found %: C 45.85; H 6.82. $C_9H_{16}O_5S$. Calculated %: C 45.75; H 6.83.

b) 25 grams of the hydroxy ester (XIV) and 25 g of potassium bisulfate were heated to 195-200° for 1.5 hours in a 25-30 mm vacuum. The reaction product was distilled at 110-156°, together with the water. The residue was dissolved in water and extracted with ether, together with the distillate. The product was washed with water, dried with magnesium sulfate, and fractionated in vacuo. This yielded 17 g of a mixture of the unsaturated esters (XIX) and (XX) with a b.p. of 117-124° at 4 mm; n_D^{26} 1.5060.

A narrow fraction in the form of a slightly yellowish liquid was isolated from this mixture for analysis:

B.p./3.5 mm 115-116°; n_D^{26} 1.5063; d_4^{20} 1.0619; MR 59.99; calculated 59.95.

6.540 mg substance: 14.750 mg CO_2; 5.000 mg H_2O; 2.890 mg SO_4. 4.640 mg substance: 10.440 mg CO_2; 3.540 mg H_2O; 2.013 mg SO_4. Found %: C 61.55, 61.40; H 8.55, 8.53; S 14.75, 14.48. $C_{11}H_{18}O_2S$. Calculated %: C 61.64; H 8.47; S 14.96.

After the unsaturated esters (XIX) and (XX) had been driven off, the 0.5 g of residue crystallized in part upon standing. This residue yielded about 0.1 g of 2,5-dimethyl-$\Delta^{4,5}$-dihydro-4-thiopyranacetic acid (IX) as colorless scales, with an m.p. of 88-89° (from water).

6.052 mg substance: 12.905 mg CO_2; 4.100 mg H_2O; 3.155 mg SO_4. 5.805 mg substance: 12,376 mg CO_2; 3.971 mg H_2O; 2.968 mg SO_4. Found %: C 58.19, 58.18; H 7.58, 7.65; S 17.40, 17.07. $C_9H_{14}O_2S$. Calculated %: C 58.03; H 7.57; S 17.21.

0.1 gram of this acid (m.p. 88-89°) was dissolved in 13 ml of glacial acetic acid, and 0.15 ml of 30% perhydrol was added to the solution. Three days later the solution was diluted with water, the water and the acetic acid driven off in vacuo, and the product extracted with ether. This yielded about 0.1 g of the sulfone (XI), which had an m.p. of 146-147° after recrystallization from water and exhibited no depression of the mixed melting point with the sample described above.

Saponifying the unsaturated esters (XIX) and (XX). 15.15 grams of a mixture of the unsaturated esters (b.p. of 117-124° at 4mm) was dissolved in 41 ml of 10% alcoholic potassium hydroxide. A half an hour later the alcohol was driven off in vacuo, the residue being dissolved in 30 ml of water and extracted with ether. Drying and distillation of the ether solution yielded 4.6 g of the unreacted ester (b.p. 117-122° at 4 mm; n_D^{20} 1.5105). Evaporation, acidulation, and ether extraction of the aqueous salt solution yielded 8.5 g of a mixture of the unsaturated acids (IX) and (XXII) with a b.p. of 150-153° at 4 mm; n_D^{20} 1.5335. The following fraction was collected from this mixture for analysis:

B.p./3 mm 146-147°; n_D^{20} 1.5325; d_4^{20} 1.1374; MR 50.78; calculated 50.60:

0.1683 g substance: 8.70 ml 0.1 N KOH.
4.992 mg substance: 3.493 mg H_2O; 10.541 mg CO_2; 2.558 mg SO_4. 4.856 mg substance: 3.392 mg H_2O. 10.271 mg CO_2; 2.462 mg SO_4. Found: M 193.54; %: C 57.62, 57.72; H 7.83, 7.81; S 17.10, 16.93. $C_9H_{14}O_2S$. Calculated: M 186.26; %: C 58.03; H 7.57; S 17.21.

The unreacted unsaturated ester (4.6 g) was resaponified with 14 ml of a 10% alcoholic solution of potassium hydroxide. The customary processing yielded 2 g of 2,5-dimethyltetrahydro-4-thiopyrylideneacetic acid (XXII) as colorless needles with an m.p. of 111-112° (from petroleum ether).

4.645 mg substance: 9.923 mg CO_2; 3.248 mg H_2O; 2.380 mg SO_4. 5.141 mg substance: 10.944 mg CO_2; 3.560 mg H_2O; 2.640 mg SO_4. Found %: C 58.30, 58.10; H 7.82, 7.75; S 17.10, 17.14. $C_9H_{14}O_2S$. Calculated %: C 58.03; H 7.57; S 17.21.

Oxidizing 2,5-dimethyltetrahydro-4-thiopyrylideneacetic acid to a sulfone (XXIII). a) 0.2 gram of the unsaturated acid (XXII) (m.p. 111-112°) was dissolved in 26 ml of glacial acetic acid, and 0.3 ml of 30% perhydrol was added to the solution. Two days later the acetic acid was driven off in vacuo, the residue being diluted with water and extracted with ether. The resultant sulfone (XXIII) had an m.p. of 197-198° (from water).

3.948 mg substance: 7.118 mg CO_2; 2.355 mg H_2O; 1.730 mg SO_4. 5.123 mg substance: 9.207 mg CO_2; 3.079 mg H_2O; 2.241 mg SO_4. Found %: C 49.20, 49.05; H 6.67, 6.72; S 14.62, 14.61. $C_9H_{14}O_4S$. Calculated %: C 49.52; H 6.46; S 14.69.

b) 1 gram of the mixture of the unsaturated acids (IX) and (XXII) (b.p. 153-160° at 4 mm) described above was dissolved in 130 ml of glacial acetic acid, and 1.5 ml of 30% perhydrol was added to the solution. Four days later the acetic acid was driven off in vacuo, and the reaction product was allowed to stand 8 days in an open container. The resultant oily liquid was washed with ether and dissolved in alcohol, the crystals that settled out the following day being filtered out and recrystallized from water. The resultant sulfone (XXIII) had an m.p. of 197-198° and exhibited no depression when mixed with the previous sample.

Anilide of 2,5-dimethyltetrahydro-4-thiopyrylideneacetic acid (XXIV). a) 0.5 gram of the unsaturated acid (XXII) (m.p. 111-112°) and 1.5 g of aniline were refluxed together for 10 hours. The anilide of 2,5-dimethyltetrahydro-4-thiopyrylideneacetic acid (XXIV) produced by the customary processing had an m.p. of 154° (from alcohol).

6.320 mg substance: 0.316 ml N_2 (25°, 744 mm). 6.638 mg substance: 0.327 ml N_2 (25°, 744 mm). Found %: N 5.61, 5.56. $C_{15}H_{19}ONS$. Calculated %: N 5.28.

b) 1.5 g of the mixture of the unsaturated acids (IX) and (XXII) (b.p. 153-160° at 4 mm) and 6 g of aniline were refluxed together for 13 hours. The customary processing yielded 0.8 g of the anilide (XIV) with an m.p. of 153-154°, which exhibited no depression when mixed with the preceding sample.

Ozonating 2,5-dimethyltetrahydro-4-thiopyrylideneacetic acid. Ozonized oxygen (8% ozone) was passed through a solution of 0.4 g of the acid (XXII) (m.p. 111-112°) in 50 ml of chloroform for 1.5 hours at the rate of 5 liters per hour. The ozonide was hydrolyzed by heating it in water (6 hours at 60°), the customary treatment of the neutral products yielding 0.15 g of the sulfone (IV), whose m.p. was 138° after recrystallization from alcohol, exhibiting no depression when mixed with a known sample.

Dehydrating the hydroxy acids (XIV). 3.5 grams of the steroisomeric hydroxy acids (XVI), produced by saponifying the esters (XIV), was heated to 200-220° for 1.5 hours in a 15-mm vacuum together with 3.5 g of potassium bisulfate. The customary processing yielded 1.3 g of the unsaturated acids (IX) and (XXII) described above, with a b.p. of 148-154° at 4 mm; n_D^{20} 1.5305. These acids (1.3 g) were boiled for 12 hours with 2 g of aniline. This yielded 0.4 g of the anilide of 2,5-dimethyltetrahydro-4-thiopyrylideneacetic acid (XXIV), which had an m.p. of 154° and exhibited no depression when mixed with the sample described above.

SUMMARY

Condensation of 2,5-dimethyltetrahydro-1-thiopyran-4-one (I) with ethyl cyanacetate and bromoacetate produced high yields of the thiopyran esters (II) and (XIV). Saponifying the ethyl thiopyrylidenecyanacetate (II) yielded the acid (V), which was decarboxylated by heat (to 170-180°), while the double bond was shifted to the ring and a mixture of the isomeric nitriles (VI) and (VII) was produced. Saponifying these nitriles yielded the dihydrothiopyranacetic acids (VIII) and (IX), which were oxidized to the corresponding crystalline sulfones (X) and (XI).

When the hydroxy ester (XIV) was saponified, we obtained two stereoisomeric hydroxy acids (XVI), the thiopyrylideneacetic acid (XXII), together with a trace of the acid (IX), being the principal product of their dehydration. When the hydroxy acid (XIV) was dehydrated, the principal product again was an unsaturated ester (XIX) with a semicyclic double bond, saponification of which yielded the acid (XXII) with a small percentage of the unsaturated ester (XX), with a double bond in the ring. The unsaturated esters (II), (XIX), and (XX), the acids (VIII), (IX), and (XXII), and the sulfones (X), (XI) and (XXIII) are not hydrogenated in alcohol, dioxane, and acetic acid solutions by Pt and Pd catalysts, even at 100°.

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Received July 29, 1950.

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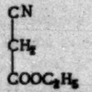
RESEARCH ON SUBSTITUTION DERIVATIVES OF ETHYL CYANACETATE AND OF THE PRODUCTS OF THEIR INTERACTION WITH ACETYLMETHYLUREA

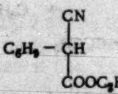
N. V. Khromov-Borisov and I. M. Yurist

The ethyl esters of cyanacetic (I), cyclohexenylcyanacetic (II), and methylcyclohexenylcyanacetic (III) acids are intermediate products in the synthesis of the sodium salt of 5-cyclohexenyl-3,5-dimethylbarbituric acid or hexenal (IV).



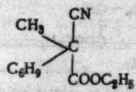
$NC-CH_2-COOC_2H_5$

(I)

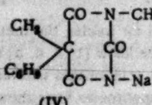


$C_6H_9-CH(CN)-COOC_2H_5$

(II)



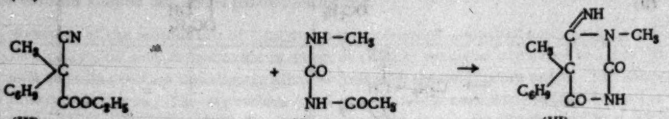
(III)



(IV)

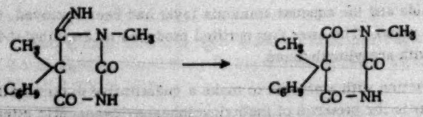
In industrial production the ethyl methylcyclohexenylcyanacetate (III) produced by methylating ethyl cyclohexenylcyanacetate (II) usually contains the initial unmethylated ester as an impurity, since these esters have adjacent boiling points and thus are hard to separate by fractionation. As a result the methylcyclohexenylcyanacetic ester used in the condensation with acetylmethylureau (V) usually contains 10-12% of the cyclohexenylcyanacetic ester.

When reacted with acetylmethylurea, the former (III) yields 5-cyclohexenyl-4-imino-3,5-dimethylbarbituric acid (VI):



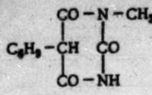
(III) (V) (VI)

which are dissolved in the cold (0-5°) in dilute hydrochloric acid, the hydrochloric acid solution being converted by heat into 5-cyclohexenyl-3,5-dimethylbarbituric acid (VII), which is precipitated out:



(VI) (VII)

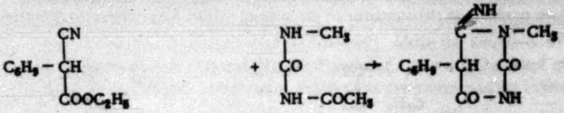
When the unmethylated ester (II) is reacted with acetylmethylurea (V), we get a solid that is insoluble in dilute mineral acids, is not saponified by heating with acids, and constitutes a waste product. The hypothesis advanced by some researchers that this substance is 5-cyclohexenyl-3-methylbarbituric acid (VIII) seemed to us to be unlikely for the following reasons. It has been established [1, 2] that the condensation of cyanacetates



(VIII)

and their derivatives with methylurea and its derivatives yields 3-methyl-4-iminobarbituric acids, which can be converted into the corresponding barbituric acids only by subsequent saponification in an acid medium. It was hard to suppose that 3-methyl-4-imino-5-cyclohexenylbarbituric acid (IX) can be saponified by hydrochloric acid without the use of heat. Thus the structure of this compound remained indeterminate.

This product was collected, purified, and indentified to establish its structure. The product had an m.p. of 195-196° after repeated recrystallizations from alcohol. The elementary analysis indicated that its composition of ($C_{11}H_{15}O_2N_3$) corresponded to 3-methyl-4-imino-5-cyclohexenylbarbituric acid. We synthesized this acid by condensing the cyclohexenylcyanacetic ester (II) with acetylmethylurea (V). The synthesized product's m.p. was 195-196° after crystallization from alcohol, while its elementary composition corresponded to the same formula of $C_{11}H_{15}O_2N_3$. The mixed melting point of the two substances indicated no depression. Hence, the condensation by-product was identified as 3-methyl-4-imino-5-cyclohexenylbarbituric acid (IX), produced by the condensation of the cyclohexenylcyanacetic ester (II), contained in the methylcyclohexenylcyanacetic ester (III), with acetylmethylurea (V):

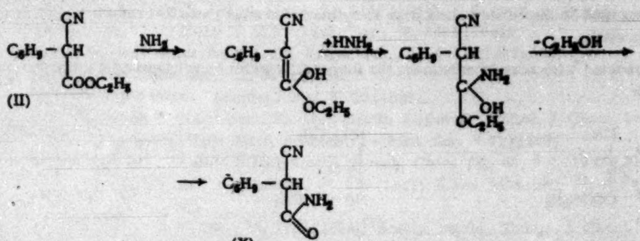


(II) (V) (IX)

The sodium salt of 3-methyl-4-imino-5-cyclohexenylbarbituric acid proved to be more toxic than hexenel when tested on rabbits and possessed no soporific action.

The question then arose of developing a method for freeing the methylcyclohexenylcyanacetic ester from the cyclohexenylcyanacetic ester it contained. We know [1, 3, 4, 5] that unsubstituted and monosubstituted malonic, acetoacetic, and cyanacetic esters form acid amides with ammonia, while the corresponding disubstituted esters do not react with ammonia. Our experiments have shown that the action of aqueous ammonia upon a mixture of the cyclohexenylcyanacetic and methylcyclohexenylcyanacetic esters converts the former into the amide (X) while the latter remains unaffected.

The following diagram may explain the interaction of the cyclohexenylcyanacetic ester with ammonia:



(II)

(X)

This diagram explains why such a reaction is impossible with disubstituted esters.

After the precipitated amide and the aqueous ammonia layer had been removed, the ester was dried with calcium chloride and distilled in vacuo. The ester thus purified produced no 3-methyl-4-imino-5-cyclohexenylbarbituric acid when condensed with acetylmethylurea.

We also employed this reaction with ammonia to make a quantitative determination of the cyanacetic and cyclohexenylcyanacetic esters in the presence of methylcyclohexenylcyanacetic ester. The accuracy of the analysis method we have elaborated is ±0.5%.

It should be pointed out at this juncture that when pure (95-96%) cyclohexenylcyanacetic ester and a fraction that contains only 10-12% of this ester are treated with concentrated aqueous ammonia, we get compounds whose composition is the same, but whose melting points differ (192-193° with decomposition and 115-116°, respectively). The titration data indicate that both compounds are produced by the reaction of 1 mole of the cyclohexenylcyanacetic ester with 1 mole of ammonia. Their elementary analysis shows that both compounds are amides of cyclohexenylcyanacetic acid. It may be that the resultant amide is condensed when the pure cyclohexenylcyanacetic ester is reacted with ammonia, whereas the reaction of ammonia with the

the cyclohexenylcyanacetic ester with 1 mole of ammonia. Their elementary analysis shows that both compounds are amides of cyclohexenylcyanacetic acid. It may be that the resultant amide is condensed when the pure cyclohexenylcyanacetic ester is reacted with ammonia, whereas the reaction of ammonia with the cyclohexenylcyanacetic ester dissolved in ten times its weight of methylcyclohexenylcyanacetic ester involves no condensation.

EXPERIMENTAL

1. Synthesis of 3-methyl-4-imino-5-cyclohexenylbarbituric acid (IX). 19.3 grams of cyclohexenylcyanacetic ester and 11.6 g of acetylmethylurea were added to a solution of 2.3 g of metallic sodium in 25 ml of absolute methanol. Condensation was effected at 65° for 6 hours in a closed vessel fitted with a reflux condenser. The solvent was driven off in vacuo (30-50 mm), the temperature of the mass being 50-60°. The residue was dissolved with cold water (60 ml), and the oily by-product of the reaction was separated. The aqueous layer was chilled to 0° and neutralized with chemically pure hydrochloric acid until its reaction was neutral. The precipitate was suction-filtered, washed with water, and crystallized twice from 50% alcohol. M.p. 195-196°.

The elementary composition confirmed that 3-methyl-4-imino-5-cyclohexenylbarbituric acid had been formed.

4.564 mg substance: 10.111 mg CO_2; 2.870 mg H_2O. 4.478 mg substance: 9.900 mg CO_2: 2.804 mg H_2O. 2.522 mg substance: 0.426 ml N_2 (19°, 743 mm). 1.746 mg substance: 0.297 ml N_2 (20.5°, 740 mm). Found %: C 60.42, 60.29; H 7.04, 7.01; N 19.31, 19.33. $C_{11}H_{15}O_2N_3$. Calculated %: C 59.73; H 6.79; N 19.00.

3-Methyl-4-imino-5-cyclohexenylbarbituric acid is soluble in hot water and when heated in dilute hydrochloric and sulfuric acids, settling out unchanged when the solutions cool. It is soluble in the cold in dilute alkali solutions (both aqueous and alcoholic), settling out again when the solutions are acidulated. When an alkaline solution is heated, the characteristic odor of cyclohexanone is perceptible.

Attempts to methylate 3-methyl-4-imino-5-cyclohexenylbarbituric acid with methyl iodide in the presence of sodium ethylate yielded the original product unchanged, m.p. 195-196°. Heating the 3-methyl-4-imino-5-cyclohexenylbarbituric acid to 150° in a sealed tube with 10% hydrochloric acid yielded a reaction product that fused over a wide range (144-155°) after recrystallization from alcohol and contained anywhere from 14 to 17% of nitrogen, depending upon the run. These findings indicate that 3-methyl-4-imino-5-cyclohexenylbarbituric acid is saponified with difficulty even under pressure; in our tests we obtained various mixtures of the initial iminobarbituric acid and its saponification product.

The reaction of the 3-methyl-4-imino-5-cyclohexenylbarbituric acid with sodium nitrite in glacial acetic acid likewise yielded the initial product unchanged.

2. Synthesis of the sodium salt of 3-methyl-4-imino-5-cyclohexenylbarbituric acid. A solution of 0.18 g of chemically pure sodium hydroxide in 40 ml of absolute methanol was added to 1 g of the iminobarbituric acid until its reaction was slightly alkaline (test with thymolpthalein paper). The alcohol was driven off in vacuo to dryness. The dry residue (1.15 g) was a white amorphous powder that was readily soluble in water. Acidulating the solution threw down the original iminobarbituric acid (m.p. 195°). Comparison of the 3-methyl-4-imino-5-cyclohexenylbarbituric acid with the by-product obtained in the synthesis of hexenal indicated the two substances were identical. The by-product had an m.p. of 195-196° after recrystallization from 50% alcohol; its mixed melting point with 3-methyl-4-imino-5-cyclohexenylbarbituric acid exhibited no depression.

0.1523 g substance: 0. 3352 g CO_2; 0.0972 g H_2O. 0.3214 g substance: 44.0 ml 0.1 N H_2SO_4. 0.1820 g substance: 25.0 ml 0.1 N H_2SO_4. Found %: C 60.01; H 7.09; N 19.17, 19.23. $C_{11}H_{15}O_2N_3$. Calculated %: C 59.73; H 6.79; N 19.00.

3. Preparation of the pure methylcyclohexenylcyanacetic ester (III). The methylated ester fraction (b.p. 140-147° at 15 mm) was treated with an equal weight of concentrated ammonia at room temperature for 6-7 hours in a vessel fitted with a stirrer. The precipitate was suction-filtered, and the oily layer separated, dried with calcium chloride, and fractionated in vacuo. A 136-138° fraction at 14-15 mm was collected. The specific gravity of the methylcyclohexenylcyanacetic ester produced was d_{20}^{20} 1.036. The yield was 80% of the processed fraction. The methylcyclohexenylcyanacetic ester thus produced no longer reacted with ammonia; condensing it with acetylmethylurea yielded 3,5-dimethyl-4-imino-5-cyclohexenylbarbituric acid that contained no 3-methyl-4-imino-5-cyclohexenyl-barbituric acid as an impurity.

4. Identification of the amide of cyclohexenylcyanacetic acid (X). a) The solid filtered out during the refining of the ester mixture with ammonia was collected, washed with water, and recrystallized repeatedly from alcohol, and finally from a mixture of alcohol and chloroform. M.p. 115-116°.

0.1648 g substance: 0.3898 g CO_2; 0.1018 g H_2O. 0.1512 g substance: 18.20 ml 0, 1 N H_2SO_4.
Found %: C 65.1; H 6.79; N 16.9. $C_9H_{12}ON_2$, Calculated %: C 65.86; H 7.32; N 17.07.

b) 10 grams of the cyclohexenylcyanacetic ester was processed with 10 g of 25% aqueous ammonia for 6-7 hours in a flask fitted with a stirrer. The mixture was diluted with water (25 ml), the precipitate filtered out, and crystallized repeatedly, first from 70% alcohol and then from a 1:1 mixture of alcohol and chloroform. The m.p. of the resulting white, crystalline substance was 192-193° with decomposition.

0.3020 g substance: 0.7230 g CO_2; 0.2026 g H_2O. 0.2138 g substance: 26.40 ml 0.1 N H_2SO_4.
Found %: C 65.2; H 7.45; N 17.29. $C_9H_{12}ON_2$. Calculated %: C 65.86; H 7.32; N 17.07.

5. Quantitative determination of the cyclohexenylcyanacetic ester. Exactly 5.0 ml of 1N aqueous ammonia was added (from a buret) to a quantity of cyclohexenylcyanacetic ester (0,2-0.3 g) placed in a conical flask with a ground-glass stopper. The mixture was chilled in a salt-ice mixture, and 5 ml of alcohol was added, after which the whole was shaken up and allowed to stand for 12 hours. Then the ammonia was back-titrated with 0.1N hydrochloric acid in the presence of methyl red. Before titration the flask was again chilled to prevent the loss of any ammonia. A blank test was run in parallel.

The method is also suitable for determining the cyanacetic acid, the time the mixture stands then being cut to 1-1.5 hours.

The results of our determination of the cyanacetic and cyclohexenylcyanacetic esters, as well as of artificial mixtures of cyclohexenylcyanacetic and methylcyclohexenylcyanacetic esters, are tabulated in Tables 1, 2, and 3.

TABLE 1
Determination of Cyanacetic Ester 1)

Test No.	Grams of cyanacetic ester used	Ml of 0.1N hydrochloric acid	% of cyanacetic ester found
1	0.1048	9.25	99.7
2	0.1782	16.65	99.2
3	0.2290	20.20	99.6
4	0.3680	32.30	99.1
5	0.3926	34.50	99.3
6	0.1800	15.75	98.9
7	0,2192	19.40	99.5
		Average	99.3

1) B.p. 96-97° at 15-16 mm. Ester content: 1) 99.8% by saponification number; 2) 99.9% by nitrogen content (Kjeldahl).

TABLE 2
Determination of Cyclohexenylcyanacetic Ester 2)

Test No.	Grams of cyclohexenylcyanacetic ester used	Ml of 0.1N hydrochloric acid	% of cyclohexenylcyanacetic ester found
1	0.2570	12.70	95.3
2	0.2600	12.70	94.2
3	0.2312	11.40	95.1
4	0.3192	15.60	94.3
5	0.2230	10.90	94.3
		Average	94.6

2) B.p. 165-167° at 15-16 mm. Ester content: 1) 95.4% by saponification number; 2) 95.8% by nitrogen content (Kjeldahl).

The figures in Table 3 indicate that the methylcyclohexenylcyanacetic ester hardly reacts with ammonia at all. The deviations of the experimental values from the quantities used lie within the limits of experimental error, totaling no more than 0.3% abs.

SUMMARY

1. The solid by-product of the synthesis of hexenal has been isolated and identified as 3-methyl-4-imino-5-cyclohexenylbarbituric acid.

TABLE 3

Determination of Cyclohexenylcyanacetic Ester in Artificial Mixtures Composed of Cyclohexenylcyanacetic Ester (B.p. 165-167° at 15-16 mm; Ester Content 94.6%) and Methylcyclohexenylcyanacetic Ester (B.p. 136-138° at 14-15 mm; Ester Content 97%)

Test No.	Grams of cyclohexenylcyanacetic ester used	Grams of methylcyclohexenylcyanacetic ester used	Ml of 0.1N hydrochloric acid	% of cyclohexenylcyanacetic ester found	% of cyclohexenylcyanacetic ester used
1	0.3690	0.2592	18.10	55.1	55.3
2	0.1764	0.3276	8.70	33.3	33.1
3	0.1712	0.3142	8.35	33.2	33.3
4	0.1028	0.4040	5.10	19.4	19.2
5	0.0422	0.3424	2.10	10.2	10.4
6	0.0608	0.7942	3.00	7.0	6.7
7	–	0.4272	0.05	0.2	0.0
8	0.0384	0.7206	1.90	4.8	4.7
9	–	0.2600	0.05	0.4	0.0
10	–	0.4454	0.05	0.2	0.0

2. It has been found that 3-methyl-4-imino-5-cyclohexenylbarbituric acid is produced by the condensation of cyclohexenylcyanacetic ester with acetylmethylurea.

3. It has been found that the methylcyclohexenylcyanacetic ester that contains no cyclohexenyl cyanacetic ester does not yield a solid by-product during its condensation with acetylmethylurea.

4. A method is suggested for preparing pure methylcyclohexenylcyanacetic ester, involving the processing of the technical ester mixture with aqueous ammonia.

5. A method has been developed for quantitatively determining cyclohexenylcyanacetic ester when methylcyclohexenylcyanacetic ester is present.

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Received August 4, 1950.

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XXXVIII. THE MECHANISM INVOLVED IN THE CATALYTIC DEHYDRATION OF FURANIDINE WITH SECONDARY AMINES

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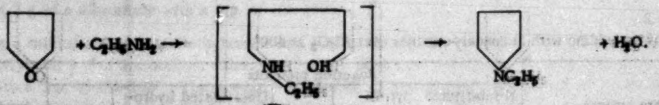
In one of our previous papers we determined that N-ethylpyrrole or N-ethylpyrrolidine is produced when furan or furanidine, respectively, is reacted with diethylamine at 400-450° over alumina; in the case of N-ethylpyrrolidine ethylene and ethylamine are also produced. Two equations were proposed by way of explaining this reaction.

1) When a mixture of furanidine and diethylamine is placed in contact with Al_2O_3 at 400°, the diethylamine is hydrolyzed by water:

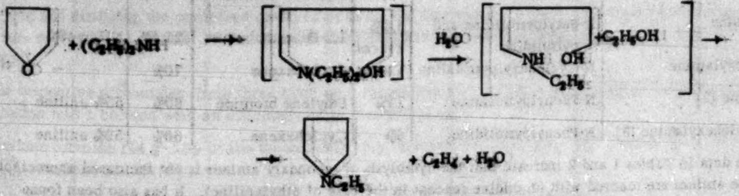
$$(C_2H_5)_2NH + H_2O \rightarrow C_2H_5OH + C_2H_5NH_2. \quad \text{(I)}$$

The ethyl alcohol produced is dehydrated, yielding ethylene, while the reaction of the ethylamine with the furanidine yields N-pyrrolidine (II) [2]:



(II)

2. When furanidine is reacted with diethylamine over Al_2O_3, 4-diethylaminobutanol-1 is formed at first, but is then hydrolyzed to 4-ethylaminobutanol-1, dehydration of which yields N-ethylpyrrolidine:



(III)

The second reaction sequence seemed to be more likely, since only a negligible amount of ethylene was produced when either pure diethylamine or a mixture of the latter with water is passed over alumina, the amount being less than when a mixture of diethylamine and furanidine is massed over the catalyst. We therefore believed that the formation of large quantities of ethylene when furnanidine and diethylamine were reacted was due to hydrolysis of the intermediate 4-diethylaminobutanol-1 (III), and not to hydrolysis of the diethylamine (I) itself.

The present paper discusses the mechanism involved in the combined catalytic dehydration of furanidine and secondary amines. Several secondary aliphatic and aliphatic-aromatic amines were hydrolyzed by contact with Al_2O_3 at 400°, the resulting unsaturated hydrocarbons being isolated and identified, while the gaseous products were converted into dibromides (Table 1). The data in Table 1 indicate that secondary amines undergo hydrolysis.

TABLE 1
Hydrolysis of Secondary Amines Over Al_2O_3 at 400°

Secondary amines	Hydrolysis products				Remarks
	Unsaturated hydrocarbons or their dibromides	Yield	NH_3 or primary amines	Yield	
Diethylamine	Ethylene bromide	25%	NH_3	54%	Dibromobutane and 1,2,3,4-tetrabromobutane were also found
Dibutylamine	1,2-Dibromobutane	48.5%	NH_3 Monobutylamine	73% Picrate	–
Dicyclohexylamine	Cyclohexene	70%	–	–	–
Ethylamine	Ethylene bromide	37%	Aniline	58%	12% of the unchanged ethylaniline
Phenylcyclohexylamine	Cyclohexene	66%	Aniline	57%	Traces of diphenylamine
Phenylcyclohexylamine + H_2O	Cyclohexene	54.5%	Aniline	78%	–

The yield of the N-alkyl or N-aryl pyrrolidines (Table 2) when they are synthesized from furanidine and secondary amines is inversely proportional to the degree of hydrolysis of the secondary amine, apparently because it is mainly the hydrolysis of the secondary amine that occurs above the catalyst.

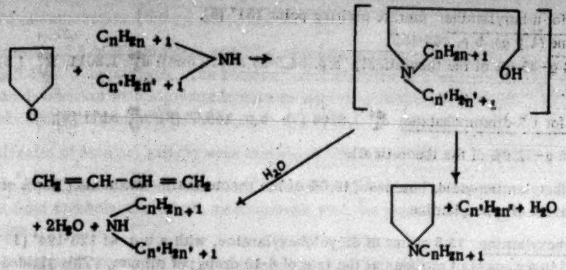
TABLE 2
Reaction of Furanidine with Secondary Amines over Al_2O_3 at 400°

Secondary amines	Reaction products				Remarks
	N-substituted pyrrolidines	Yield	Unsaturated hydrocarbons or their dibromides	Yield	
Diethylamine [1]	N-Ethylpyrrolidine	29%	Ethylene bromide	9.4%	–
Dibutylamine	N-Butylpyrrolidine and pyrrolidine	4.5% Traces	1,2-Dibromobutane	21.5%	NH_3 – 48%
Dicyclohexylamine	N-Cyclohexylpyrrolidine	Traces	Cyclohexene	70%	–
Ethylaniline [2]	N-Phenylpyrrolidine	11%	Ethylene bromide	60%	55% aniline
Phenylcyclohexylamine [3]	N-Phenylpyrrolidine	6%	Cyclohexene	60%	59% aniline

The data in Tables 1 and 2 indicate that the hydrolysis of secondary amines is not increased appreciably when these amines are reacted with furanidine (except in the case of ethylaniline). It has also been found that diphenylamine does not react with furanidine: 75% of the unchanged diphenylamine was recovered from the catalyzate produced when a mixture of furanidine and diphenylamine was passed over Al_2O_3 at 400°. No N-phenylpyrrolidine was produced. Thus, a secondary amine whose hydrolysis is hampered does not react with furanidine.

Lastly, if the reaction were to follow the second schema, the hydrolysis of the intermediate tert-aminobutanol ought to result in the production of more divinyl than is produced by the dehydration of pure furanidine over alumina (or by the hydrolysis of a 4-alkylaminobutanol-1), since it is easier to hydrolyze tertiary amines than secondary or primary amines: (see diagram top of next page).

The amount of divinyl produced when furanidine was passed over alumina at 400° proved to be just as small, however, as when furanidine was reacted with ethylamine or diphenylamine. We, therefore, conclude, contrary to our previous position, that when furanidine is reacted with secondary amines over Al_2O_3 at 400°, the secondary amine is first hydrolyzed, the resulting primary amine (I and II) reacting with the furanidine, i.e., that the first of the schemas set forth above for the mechanism involved in this reaction is correct.



EXPERIMENTAL

I. Hydrolysis of Secondary Amines over Al_2O_3

1. Hydrolysis of diethylamine. a) 10 grams of diethylamine was passed over alumina at 400° in a current of nitrogen at a rate of 6-8 drops per minute. The catalyzate was collected in a well-chilled receiver, which was connected to a wash bottle containing dilute hydrochloric acid and two wash bottles containing bromine. Three ml of catalyzate was collected in the receiver. Evaporating the hydrochloric acid solution yielded 4.3 g of ammonium chloride. The bromine was driven off from the contents of the bromine bottles, which were then washed with water, dried with calcium chloride, and double-distilled, yielding the following two fractions: b.p. 130-135°—5 g; and b.p. 135-160°—4.3 g.

b) A mixture of 10 g of diethylamine and 2.5 ml of water was passed over alumina under the same conditions. This yielded: 4 g of moist catalyzate, 4 g of ammonium chloride, 14 g of a dibromide with a b.p. of 129-135°, and 4.7 g of a dibromide with a b.p. of 135-155°.

c) Processing a mixture of 14 g of diethylamine and 4 ml of water under the same conditions yielded: 5 ml of moist catalyzate, 5 g of ammonium chloride, 23 g of a dibromide with a b.p. of 129-135°; and 6.2 g of a dibromide with a b.p. of 135-160°. The residue left after the dibromides had been driven off crystallized; its m.p. was 117-118° after recrystallization from petroleum ether, and it proved to be 1,2,3,4-tetrabromobutane. Its mixed melting point with pure 1,2,3,4-tetrabromobutane was 117-117.5°, exhibiting no depression.

Figures in the literature for 1,2,3,4-tetrabromobutane: m.p. 116-119° [4]; m.p. 116-117° [5].

Drying and distilling the combined catalyzates of all the runs yielded 1.8 g of unchanged diethylamine, with a b.p. of 55-60°. A total of 13.3 g of ammonium chloride was collected from all the runs (54.4% of the theoretical).

The respective dibromides (from three runs) were mixed together, yielding the following compounds after fractionation into a column with an efficiency of 18 theoretical trays:

Ethylene bromide (44 g—25% of the theoretical): b.p. 128.5-129.5° (742 mm); n_D^{20} 1.5384; d_4^{20} 2.1695; MR_D 27.11; calculated 26.96;

High-boiling bromide (2.5 g): b.p. 157.5-159° (742 mm); n_D^{20} 1.5160; d_4^{20} 1.8282.

43.186 mg substance: titration of 0.1 part by weight consumed 2.007 mg of a 0.02N solution of $AgNO_3$.
28.720 mg substance: titration of 0.1 part by weight consumed 1.332 ml of a 0.02N solution of $AgNO_3$.
Found %: Br 74.30, 74.15. $C_4H_8Br_2$. Calculated %: Br 74.02.

The analysis data and the constants indicate that this dibromide is apparently dibromobutane.

Hence, passing diethylamine over alumina at 400°, either by itself or mixed with water, cleaves it, yielding ethylene (25% of the theoretical) and ammonia (54% of the theoretical).

2. Hydrolysis of dibutylamine. A mixture of 15 g of n-dibutylamine (b.p. 159°) and 2 ml of water was passed over Al_2O_3 at 400° in a current of nitrogen at a rate of 6-8 drops per minute. The reaction products were collected and isolated as described above. The following reaction products were recovered:

n-Butylamine (0.8 g), identified by preparing its picrate, m.p. 149-150°.

Figures in the literature for n-butylamine: picrate melting point 151° [6].

Unchanged n-dibutylamine (1.0 g), b.p. 157-159°.

1,2-Dibromobutane (24.4 g—48.6% of the theoretical): b.p. 54.5-55.5° (16 mm); d_4^{20} 1.8011; n_D^{20} 1.5147; MR_D 36.14; calculated 36.20.

Figures in the literature for 1,2-dibromobutane: d_4^{20} 1.8204 [7]; b.p. 166.3° [8]; n_D^{20} 5171 [9];

Ammonium chloride (4.5 g—72.6% of the theoretical).

Thus, the hydrolysis of dibutylamine yields butene-1 (48.6% of the theoretical); ammonia (72.6% of the theoretical); and a slight amount of n-butylamine.

3. Hydrolysis of dicyclohexylamine. 13.5 grams of dicyclohexylamine, with a b.p. of 123-124° (17 mm), was passed over Al_2O_3 at 400° in a current of nitrogen at the rate of 8-10 drops per minute. This yielded 10.8 g of catalyzate, distillation of which (after drying) yielded 8.5 g of cyclohexene (70% of the theoretical).

B.p. 82-83° (758 mm); n_D^{20} 1.4450; d_4^{20} 0.8113; MR_D 27.17; calculated 27.24.

Figures in the literature for cyclohexene: b.p. 84° (763 mm); d_4^{20} 0.8112; n_D^{20} 1.4469 [10].

4. Hydrolysis of ethylaniline. 46 grams of ethylaniline, b.p. 84.4-84.8° (10 mm), was passed (in 23-g portions) over Al_2O_3 at 400° in a current of nitrogen at the rate of 6-8 drops per minute. The receiver was connected to a wash bottle containing bromine. Drying the catalyzate and double-distilling it in vacuo yielded:

Aniline (16.7 g—58.2% of the theoretical): b.p. 72-73° (11 mm); n_D^{20} 1.5827; m.p. of acetanilide 114-115°.

Ethylaniline (5.5 g — 12% of the amount placed in reaction).

The contents of the flask containing bromine yielded 26.6 g of ethylene bromide (37.0% of the theoretical), b.p. 130.5-131.5° (760 mm); n_D^{20} 1.5345.

Thus, ethylaniline is hydrolyzed substantially, yielding ethylene and aniline.

5. Hydrolysis of phenylcyclohexylamine. a) 14 g of phenylcyclohexylamine, with a b.p. of 137.5-139.5° (8 mm), was passed over alumina at 400° in a current of nitrogen at the rate of 6-8 drops per minute. This yielded 12 ml of catalyzate. The ether extract of the catalyzate was dried with potash, and the ether driven off, the residue yielding:

Cyclohexene (4.3 g—66% of the theoretical): b.p. 81.5-82.5 (750 mm); n_D^{20} 1.4428; d_4^{20} 0.8056; MR_D 27.06; calculated 27.24;

Aniline (4.2 g—57% of the theoretical): b.p. 64-65° (8 mm); n_D^{20} 1.5820; m.p. of acetanilide 114°.

Diphenylamine (0.3 g), whose melting point was 52.5° after double recrystallization from petroleum ether. Its mixed melting point with pure diphenylamine was 52-52.5°, exhibiting no depression.

b) A mixture of 12 g of phenylcyclohexylamine and 1.2 ml of water was passed over Al_2O_3 under the conditions described above. This yielded 10 ml of catalyzate, the customary processing yielding:

Cyclohexene (3 g—54.5% of the theoretical): b.p. 82-83° (762 mm); n_D^{20} 1.4442; d_4^{20} 0.8008; MR_D 27.26;

Aniline (5 g—78.0% of the theoretical): b.p. 74-76° (14 mm); n_D^{20} 1.5842.

Thus, hydrolyzing phenylcyclohexylamine by placing it in contact with Al_2O_3 yields aniline, cyclohexene, and traces of diphenylamine.

II. Reaction of Furanidine with Secondary Amines.

1. Reaction of furanidine with n-dibutylamine. a) A mixture of 10 g of furanidine and 18 g of n-dibutylamine (1:1) was passed over Al_2O_3 at 400° in a current of nitrogen at the rate of 6-8 drops per minute. This yielded 14 ml of catalyzate. The receiver was connected to a wash bottle containing dilute hydrochloric acid, followed by two wash bottles containing bromine. The usual processing of the bromides yielded:

1,2-Dibromobutane [1] (22.3 g—21.5% of the theoretical): b.p. 163-164° (750 mm); n_D^{20} 1.5137; d_4^{20} 1.7888 MR_D 36.33; calculated 36.20.

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[1] In distilling the dibromide we secured 11.7 g of first runnings with a b.p. of 140-163° (750 mm), which were apparently a mixture of 1,2-dibromobutane and 1,2-dibromopropane, the latter being formed from propylene, a decomposition product of the furanidine [1].

1,2,3,4-Tetrabromobutane (0.6 g): m.p. 116-117°.

b) A mixture of 7.5 g of furanidine and 13 g of n-dibutylamine was passed over Al_2O_3 under the same conditions, yielding 7.5 ml of catalyzate. The receiver was connected to a wash bottle containing 250 ml of 1.138N hydrochloric acid; titration with a sodium hydroxide solution established that 0.787 g of ammonia (48% of the theoretical) was evolved during the reaction.

The catalyzates of Runs (a) and (b) were combined, dried, and distilled, yielding:

Pyrrolidine (0.5 g of a fraction with a b.p. of 82-90°), whose picrate melting point was 111-112° (after recrystallization from alcohol); the mixed melting point with the picrate of pure pyrrolidine was 111-112°, exhibiting no depression.

N-butylpyrrolidine (1.4 g—4.5% of the theoretical): b.p. 151-155°; picrate melting point 124-124.5° (from alcohol).

Figures in the literature for pyrrolidine: Yu. K. Yuryev [11]: b.p. 85.8-86.8°; picrate melting point 112°; for N-butylpyrrolidine: Yu. K. Yuryev [11]: b.p. 154.5-155.5° (748.5 mm); n_D^{20} 1.4408; d_4^{20} 0.8143; picrate melting point 124°.

Thus, the reaction of furanidine with n-dibutylamine involves substantial hydrolysis of the dibutylamine, resulting in the production of butene-1, in addition to the formation of negligible quantities of N-butylpyrrolidine and pyrrolidine.

2. Reaction of furanidine with dicyclohexylamine. A mixture of 5 g of furanidine and 12 g of dicyclohexylamine was passed over Al_2O_3 at 400° under the conditions described above. The ether extract was dried with fused potassium hydroxide and the ether driven off, yielding:

Cyclohexene (7.6 g—70.0% of the theoretical): b.p. 81-83° (760 mm); n_D^{20} 1.4460; d_4^{20} 0.8107; MR_D 27.02;

N-cyclohexylpyrrolidine (0.3 g): b.p. 65-68° (5 mm); picrate melting point (from alcohol): 163-164°.

Figures in the literature for N-cyclohexylpyrrolidine: Yu. K. Yuryev [11]: b.p. 79° (8 mm): n_D^{20} 1.4888; d_4^{20} 0.9135; picrate melting point 164.5°.

No pyrrolidine was found.

Thus, only a negligible amount of N-cyclohexylpyrrolidine is produced when furanidine is reacted with dicyclohexylamine, the principal reaction product being cyclohexene (70% of the theoretical yield).

3. Reaction of furanidine with diphenylamine. A solution of 23.4 g of diphenylamine in 10 g of furanidine was passed over Al_2O_3 at 400° in a current of nitrogen at the rate of 6-8 drops per minute. The gases evolved were absorbed in bromine. The catalyzate, which crystallized in the receiver, was dissolved in ether and dried with fused alkali, the ether driven off, and the residue distilled in vacuo. This yielded 0.5 g of a fraction with a b.p. of 60-120° (5 mm) and 17.5 g of a fraction with a b.p. of 125-130° (5 mm).

The second fraction consisted of the unchanged diphenylamine (74.8% of the amount used for the reaction), which had an m.p. of 51-52° after recrystallization from petroleum ether. The fraction with a b.p. of 60-120° (5 mm) yielded acetanilide with an m.p. of 113° and a picrate, which had an m.p. of about 170° (with decomposition) after recrystallization from alcohol, evidence that this fraction contained aniline.

The contents of the flask containing bromine yielded 4.5 g of 1,2-dibromopropane (15.1% of the theoretical): b.p. 139-141° (759 mm); n_D^{20} 1.5210; d_4^{20} 1.9225; MR_D 31.98; calculated 31.58.

Recrystallization frompetroleum ether of the residue left after the 1,2-dibromopropane had been distilled yielded 0.3 g of 1,2,3,4-tetrabromobutane with an m.p. of 116-117°.

Thus, no N-phenylpyrrolidine is produced when furanidine is reacted with diphenylamine. The following reaction products were found: negligible amounts of aniline and propylene, and traces of divinyl, 75% of the diphenylamine being recovered unchanged.

4. Formation of divinyl when furanidine is reacted with ethylamine. A mixture of 6 g of ethylamine and 7.5 g of furanidine was passed over Al_2O_3 at 400°. A total of 1886 ml of gas (NTP) was collected. The gases contained 1.3% of divinyl (determined in a Korotkov apparatus [12]), in other words, furanidine is only 0.9%

dehydrated over Al_2O_3 to yield divinyl.

5. Formation of divinyl when furanidine is reacted with diphenylamine. A solution of 13 g of diphenylamine in 6 g of furanidine was passed over Al_2O_3 at 400°, yielding 1447 ml of gas (NTP). The gas contained 1% of divinyl, so that furnidine is only 0.77% dehydrated to yield divinyl (in the presence of diphenylamine).

III. Behavior of Furanidine over Al_2O_3 at 400°.

a) 10 g of furanidine was passed over Al_2O_3 at 400° in a current of nitrogen at the rate of 6-8 drops per minute. The gases evolved were absorbed in bromine. The customary processing of the contents of the bromine-filled bottles yielded:

1,2-Dibromopropane (9 g—32.2% of the theoretical): b.p. 139-140° (757 mm); n_D^{20} 1.5210; d_4^{20} 1.9323; MR_D 31.44 and 0.2 g of 1,2,3,4-tetrabromobutane with a m.p. of 117°.

b) When 10 g of furanidine was passed over the catalyst under the same conditions, we collected 3165 ml of gas (NTP), 871 ml of which was nitrogen. The composition of the gas (without the nitrogen) was as follows: 3.6% CO_2; 73% unsaturated hydrocarbons; 1.1% oxygen; 7% carbon monoxide; 6.8% hydrogen; and 8.5% saturated hydrocarbons.

c) 5.7 grams of furanidine yielded 990 ml of gas (NTP) when passed over Al_2O_3 at 400°. The divinyl totaled 1.42% (analysis in a Korotkov apparatus [12]) i.e., furanidine is 0.8% dehydrated over Al_2O_3 at 400° to yield divinyl.

Thus, furanidine is decomposed over Al_2O_3 at 400°, the principal products being propylene, carbon monoxide, carbon dioxide, and hydrogen; a small amount of divinyl is also produced.

SUMMARY

The present paper demonstrated that when furanidine is reacted with secondary amines over Al_2O_3 at 400°, the secondary amine is first hydrolyzed, the resulting primary amine then reacting with the furanidine.

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Received July 13, 1950

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SULFONATION AND SULFO ACIDS OF ACIDOPHOBIC COMPOUNDS

XIX. POLAROGRAPHIC INVESTIGATION OF PYRROLESULFONIC ACIDS

A. P. Terentyev, L. A. Yanovskaya, and Ev. A. Terentyeva

When some pyrroles, such as 1- and 2-acetylpyrrole, and 1-phenylpyrrole, are sulfonated with pyridine sulfotrioxide, beta sulfo acids are produced as well as the alpha acids [1,2]. We needed a method that would enable us to determine the isomer present in a small quantity of sulfo acid and to establish the individuality of a substance or the existence of a mixture, in order to be able to analyze the reaction products of the sulfonation of pyrroles.

None of the existing chemical methods was able to meet our needs. Although oxidation of the barium salts of pyrrolesulfonic acid with a chromic acid mixture makes it possible, in general, to determine the acid's structure and even to decide whether we are dealing with an individual substance or a mixture of isomers, the method is not very precise; possibly not all the oxidation products being collected when small quantities are being used, especially when one of the isomers predominates.

The method of solubility and lixiviation that we have employed in the past to investigate the sulfonation products of pyrrole itself [3], might serve our purpose. But this method of determining the isomers in a mixture requires that we first have the individual substances. It is not always easy to separate a mixture of isomers, the procedure requiring comparatively large quantities of the material and considerable time. In the light of these considerations we rejected this procedure.

Reviewing the entire arsenal of physicochemical methods, we were attracted to the method of polarography, which has been more and more widely utilized in organic chemistry to solve diverse problems, particularly in research on tautomerism and isomerism.

We decided to investigate the polarographic behavior of pyrrolesulfonic acids. In our research we made use of a visual polarographic setup. The rate of mercury discharge was kept constant at one drop in 5 seconds. The potentials were measured against a calomel subsidiary reference electrode with an accuracy of 0.002 volt. The electrolyte used was a half-normal solution of potassium chloride.

We found that the pyrrolesulfonic acids (in the form of their barium salts) are not reduced at a mercury dropping electrode. This forced us to attempt the polarographic oxidation of pyrrolesulfonic acids. Our very first tests showed that pyrrolesulfonic acids are readily oxidized at a mercury dropping electrode, setting up distinct polarographic waves. The present paper is a report on the results we obtained in our study of the polarographic oxidation of pyrrolesulfonic acids.

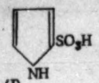
As our tests showed electrolytic oxidation is smoothest in slightly hydrochloric acid media (pH 4.2-4.7). When strongly acid media (pH below 3.7) were employed, maxima appeared on the polarographic curves that were hard to eliminate, thus interfering with measurement of the polarographic waves. Polarography in alkaline media (pH above 9) indicated that it is hard to oxidize pyrrolesulfonic acids under these conditions. The polarographic wave is indistinct in neutral media.

A single procedure was employed in all instances: a sample of the thoroughly purified barium salts of pyrrolesulfonic acids was dissolved in a previously prepared solution of 0.5N KCl–0.003N HCl, in a measuring flask, to make the concentration of the substance about 0.003N (this ensured the optimum solution pH).

Electrolytic oxidation of pyrrolesulfonic-2 acid (I). The barium salt of pyrrolesulfonic-2 acid used in polarography was recrystallized four times from a water-alcohol mixture.

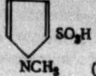
At a mercury dropping electrode pyrrolesulfonic-2 acid produces a single polarographic wave, the height of which is easily measured. The polarogram is shown in Fig. 1. The half-wave oxidation potential is 0.022 volt.

We recorded the polarograms of some other alpha sulfo acids of known structure, in addition to the pyrrolesulfonic-2 acid.



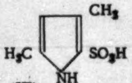
(I)

Electrolytic oxidation of 1-methylpyrrolesulfonic-2 acid (II). The barium salt we used for oxidation was recrystallized twice from a water-alcohol mixture. 1-Methylpyrrolesulfonic-2 acid exhibits a single fully developed wave (Fig. 2). The oxidation half-wave potential is 0.018 volt.



(II)

Electrolytic oxidation of 2,4-dimethylpyrrolesulfonic-5 acid (III). The barium salt of 2,4-dimethylpyrrolesulfonic-5 acid produces a single wave (Fig 3), with a half-wave oxidation potential of 0.015 volts, after thorough crystallization from a water-alcohol mixture and washing with ether.



(III)

Thus, pyrrole sulfo acids with the sulfo group in the alpha position are readily oxidized at a mercury dropping electrode and have half-wave potentials that are closely alike. One cannot fail to note that the accumulation of methyl groups lowers the potential somewhat, i.e., facilitates oxidation. This behavior rigorously conforms to the chemical properties of the pyrroles.

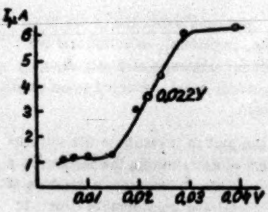


Fig. 1

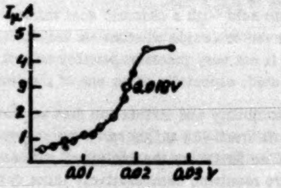


Fig. 2

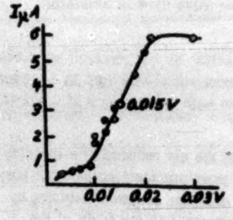


Fig. 3

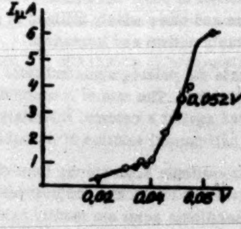
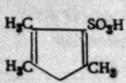


Fig. 4

We investigated the behavior of pyrrole sulfo acids with the sulfo group in the beta position by plotting the polarograms of the barium salts of 2,4,5-trimethylpyrrolesulfonic-3 and 1,2,5-trimethylpyrrolesulfonic-3 acids.

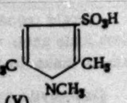
Electrolytic oxidation of 2,4,5-trimethylpyrrclesulfonic-3 acid (IV). The barium salt of 2,4,5-trimethylpyrrolesulfonic-3 acid was purified by repeated reprecipitation from an alocholic solution of ether.



(IV)

The polarogram exhibits a single wave (Fig. 4), with an oxidation half-wave potential of 0.052 volt.

Electrolytic oxidation of 1,2,5-trimethylpyrrolesulfonic-3 acid (V). Purifying the barium salt of 1,2,5-trimethylpyrrolesulfonic-3 acid required its reprecipitation from alcohol with ether no less than four or five times. The wholly pure salt exhibits a single wave and a half-wave oxidation potential of 0.044 volt (Fig. 5).



(V)

Comparing the alpha and the beta pyrrolesulfonic acids reveals a marked difference in their polarographic behavior; the beta pyrrolesulfonic acids displaying much higher oxidation potentials.

The existence of this appreciable difference in potential led us to hope that it would be possible to discriminate between alpha and beta acids in a mixture. To test this, we prepared an articifical mixture of the barium salts of pyrrolesulfonic-2 acid (I) and 2,4,5-trimethylpyrrolesulfonic-3 acid (IV), using approximately equal volumes of the ready solutions, and then polarographed the mixture. We found that the polarographic curve exhibited two distinct curves with half-wave oxidation potentials of 0.021 and 0.044 volt respectively (Fig. 6), i.e., lying within the potential regions of the pure original salts.

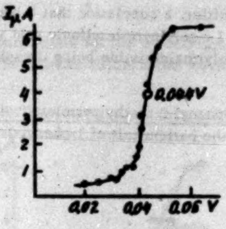


Fig. 5

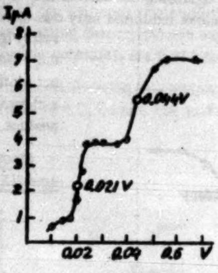


Fig. 6

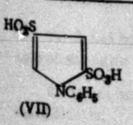
Thus, we can actually discriminate between alpha and beta pyrrolesulfonic acids polarographically in a mixture of the acids.

We then turned to a polarographic investigation of the barium salts that had proved to be heterogeneous upon chemical analysis, or which we might suspect were heterogeneous. We began by polarographing the barium salts of the sulfo acids of 1-phenylpyrrole, 1-(p-nitrophenyl)-pyrrole, 1-o-tolylpyrrole, and 1-phenyl-2-methylpyrrole.

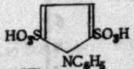
Electrolytic oxidation of 1-phenylpyrrolesulfonic acid. There are two distinct curves on the polarization curve plotted for the polarographic oxidation of 1-phenylpyrrolesulfonic acid. The half-wave oxidation potentials were 0.026 and 0.052 volt, values that lie in the range of the respective alpha and beta pyrrolesulfonic acids. These findings justified us in concluding that the 1-phenylpyrrole sulfonic acid under test is not an individual substance, but rather a mixture of the barium salts of at least two acids: 1-phenylpyrrolesulfonic-2 and 1-phenylpyrrolesulfonic-3 acids. This was a beautiful confirmation of the results of chemical analysis obtained by oxidizing 1-phenylpyrrolesulfonic acid with a chromic acid mixture.

These findings likewise dispel any doubt concerning the possible existence of a third isomer in the mixture, with the sulfo group in the benzene ring, for such an isomer would have to have its own characteristic oxidation potential, and the polarogram would therefore exhibit a third wave. The oxidation potential of a sulfo acid with the sulfo group in the benzene ring would obviously have to be much lower than that of acids in which the sulfo group is attached to the pyrrole ring, inasmuch as the negative sulfo group radical stabilizes the pyrrole ring only when it is attached to that ring itself. The presence of a sulfo group in the phenyl ring would hardly affect the molecule's resistence to oxidation.

Electrolytic oxidation of 1-phenylpyrrolesulfonic acid (VI) and (VII). This acid likewise exhibits two waves in its polarogram (Fig. 7), with half-wave oxidation potentials of 0.20 and 0.042 volt, lying in the ranges that are typical of alpha and beta sulfo acids. We may conclude from a comparison of these findings with the results of our oxidation of 1-phenylpyrrolesulfonic acid that we have here a mixture of the barium salts of isomeric sulfo acids, one obviously possessing the structure of 1-phenylpyrroledisulfonic-2,5 acid (VI). The most likely structure of the other acid is 1-phenylpyrroledisulfonic-2,4 acid (VII). It is impossible to use this method to resolve the problem of the existence of isomeric sulfo acids with one of the sulfo groups in the benzene ring, since the oxidation potential of such acids would obviously be



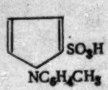
(VII)



(VI)

governed by the position of the other sulfo group at the alpha or beta position in the pyrrole ring.

Electrolytic oxidation of 1-(p-nitrophenyl)-pyrrolesulfonic acid. The polarogram of the barium salt of 1-(p-nitrophenyl)-pyrrolesulfonic acid has two waves, the half-wave oxidation potentials being 0.019 and 0.050 volt, respectively. Hence, this salt is also a mixture of isomeric salts of the alpha and beta sulfo acids.



(VIII)

Electrolytic oxidation of 1-o-tolylpyrrolesulfonic acid (VIII). By analogy with the 1-phenylpyrrolesulfonic acid we might suppose that 1-o-tolylpyrrolesulfonic acid is also a mixture. We tested this assumption by oxidizing the barium salt of 1-o-tolylpyrrolesulfonic acid with a mercury dropping electrode. The polarization curve exhibited only one wave, however, with half-wave oxidation potential of 0.024 volt (Fig. 8). This proves that this is an individual sulfo acid with the sulfo group in the alpha position, a conclusion that is borne out by the results of oxidizing 1-o-tolylpyrrolesulfonic acid with a chromic acid mixture, N-o-tolylmaleinimide being the sole product.

Electrolytic oxidation of 1-phenyl-2-methylpyrrolesulfonic acid (IX). The polarogram of the barium salt of 1-phenyl-2-methylpyrrolesulfonic acid likewise exhibits only a single wave (Fig. 9), its half-wave oxidation potential being 0.019 volt. Hence, this acid is an individual substance, with the structure of 1-phenyl-2-methylpyrrolesulfonic-5 acid. This conclusion agrees with the results of chemical oxidation.

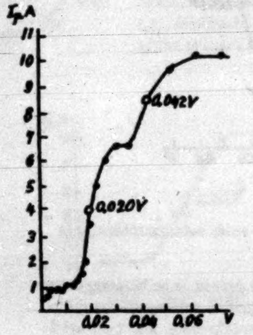


Fig. 7

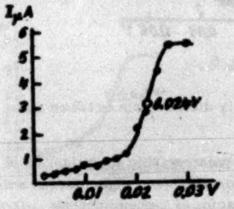
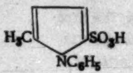


Fig. 8

After plotting the polarograms of the group of N-aryl substitution derivatives of pyrrolesulfonic acids, we turned to the polarographic study of acetylpyrrolesulfonic acids.



(IX)

Electrolytic oxidation of 1-acetylpyrroldisulfonic acid (X) and (XI). There are three distinct waves in the polarogram of 1-acetylpyrroledisulfonic acid (Fig. 10). Two of these waves lie in the potential ranges typical of alpha and beta pyrrolesulfonic acids (0.024 and 0.053 volt).

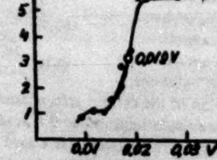


Fig. 9

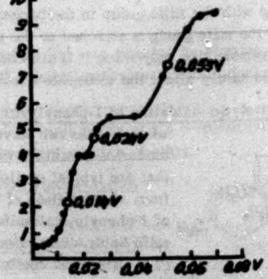
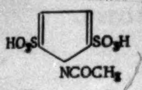
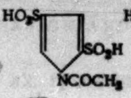


Fig. 10

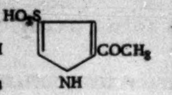
These findings are evidence that the initial substance contains at least two isomeric acids: 1-acetylpyrroledisulfonic-2,5 (X) and 1-acetylpyrroledisulfonic-2,4 (XI) acid. This conclusion agrees with the results of chemical oxidation. The genesis of the first wave with a half-wave oxidation potential of 0.014 volt is unclear.



(X)



(XI)



(XII)

Electrolytic oxidation of the 2-acetylpyrrolesulfonic acids produced by sulfonating 2-acetylpyrrole with oleum and pyridine sulfotrioxide (XII). There are two waves visible (Fig. 11) in the polarogram for the oxidation at a mercury dropping electrode of the 2-acetylpyrrolesulfonic acid prepared by sulfonating 2-acetylpyrrole with oleum. The half-wave potentials are 0.015 and 0.055 volt.

The polarogram for the 2-acetylpyrrolesulfonic acid prepared by sulfonating 2-acetylpyrrole with pyridine sulfotrioxide likewise exhibits two waves, with half-wave potentials of 0.017 and 0.053 volt (Fig 12).

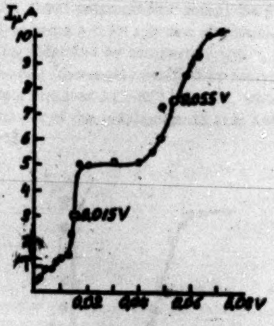


Fig. 11

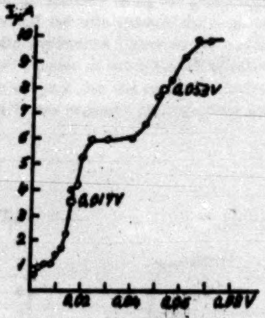


Fig. 12

It is obvious that waves with half-wave potentials of 0.055 and 0.053 volt belong to a 2-acetylpyrrolesulfonic acid with the sulfo group at the beta position (XII). We are not inclined to attribute the presence of a second wave in both of these polarograms to the existence of a second isomer in the original substances, for the polarogram of 1-acetylpyrrolesulfonic acid also exhibits a wave with a half-wave oxidation potential of 0.014 volt, a value that is extremely close to the values of 0.015 and 0.017 volt obtained for 2-acetylpyrrole sulfonic acid.

It should be noted that a certain scattering of the plotted points in the region of the potentials typical of alpha pyrrole sulfo acids is observed in the polarogram of the 2-acetylpyrrolesulfonic acid prepared by sulfonating 2-acetylpyrrole with pyridine sulfotrioxide, which indicates that the alpha isomer may be present as an impurity.

SUMMARY

1. It has been shown that the polarographic oxidation method may be employed to determine the position of the sulfo group in pyrrolesulfonic acids.

2. It has been shown that the alpha and beta pyrrole sulfo acids in a mixture can be determined polarographically.

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Received September 29, 1950 Laboratory of Organic Chemistry, The Lomonosov State University of Moscow

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*See Consultants Bureau translation, p. a-591.

**See Consultants Bureau translation, p. 539.

SULFONATION AND SULFO ACIDS OF ACIDOPHOBIC COMPOUNDS

XX. POLAROGRAPHIC INVESTIGATION OF INDOLESULFONIC ACIDS

A. P. Terentyev and L. A. Yanovskaya

The interesting results we had obtained in our study of pyrrolesulfonic acids by the polarographic oxidation method [1], impelled us to apply this method to the indolesulfonic acids.

The experiments were carried out under the same conditions as those described in our preceeding report. We used a visual polarographic setup, the discharge rate of the mercury being one drop every 5 seconds, the electrolyte being a 0.5N solution of potassium chloride, acidulated with hydrochloric acid, and the potentials being measured by comparison with a calomel subsidiary reference electrode. Barium salts of indolesulfonic acids, thoroughly purified by recrystallization from aqueous or water-alcohol solutions, were dissolved in a prepared KCl-HCl mixture, whose composition was such that the resulting solution had a 0.003 N concentration of the indolesulfonic acid and a pH of 4.2-4.7. We began by polarographing alpha indolesulfonic acids.

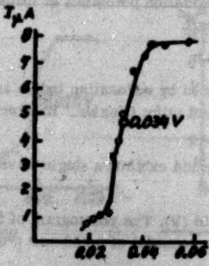


Fig. 1

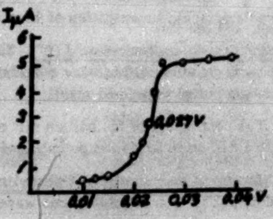
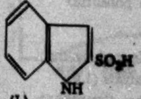


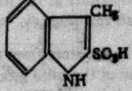
Fig. 2

Electrolytic oxidation of indolesulfonic-2-acid (I). This acid was prepared by sulfonating indole at a temperature of 110-120° [2], with pyridine sulfotrioxide that contained no excess of sulfur trioxide. The structure of the acid was established as indolesulfonic-2 acid by reacting it with a fused alkali and hydrolyzing it with hydrochloric acid, the oxindole produced being isolated and identified.



(I)

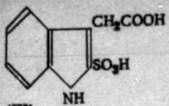
The polarogram (Fig. 1) displayed a single wave with a half-wave oxidation potential of 0.034 volt.



(II)

Electrolytic oxidation of 3-methylindolesulfonic-2 acid (II). The barium salt of 3-methylindolesulfonic-2 acid was smoothly oxidized at the mercury dropping electrode, one wave being exhibited by the polarogram. The half-wave oxidation potential was 0.027 volt (Fig. 2).

Electrolytic oxidation of 2-sulfo-3-indolylacetic acid (III). The polarogram of the barium salt of 2-sulfo-3-indolylacetic acid closely resembled the preceding one. The half-wave oxidation potential was 0.026 volt (Fig. 3).



(III)

Thus, the indolesulfonic acids with the sulfo group in the alpha position are oxidized fairly easily at a mercury dropping electrode. It is worthy of note that the half-wave oxidation potentials of alpha indolesulfonic acids are appreciably higher than the half-wave oxidation potentials of alpha pyrrolesulfonic acids (the half-wave potential of pyrrolesulfonic acid is 0.022 volt, for example, while that of indolesulfonic-2 acid is 0.034 volt). This agrees satisfactorily with the fact that indole compounds are known to be more stable than pyrrole compounds.

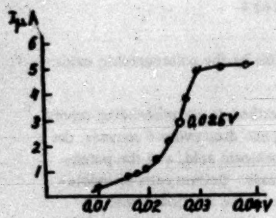


Fig. 3

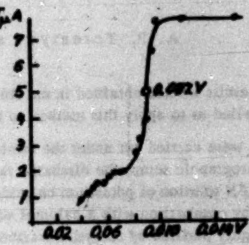
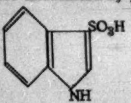


Fig. 4

It should also be pointed out that introducing methyl groups lowers the oxidation potentials of indole sulfo acids somewhat, as we found to be true of alpha pyrrole sulfo acids as well.

We then turned to polarographic investigation of beta indolesulfonic acids.

Electrolytic oxidation of indolesulfonic-3-acid (IV). This acid was prepared by sulfonating indole at a temperature of 130-140° with pyridine sulfotrioxide containing a 0.6% excess of sulfur trioxide. Its structure was established by producing indigo with fused alkali.

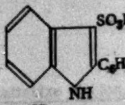


(IV)

The polarogram of the barium salt of indolesulfonic-3 acid exhibits a single wave with a half-wave oxidation potential of 0.092 volt (Fig. 4).

Electrolytic oxidation of 2-phenylindolesulfonic-3 acid (V). The polarogram of 2-phenylindolesulfonic-3 acid exhibits one wave with a half-wage potential of 0.058 volt (Fig. 5).

These findings show that the beta indole sulfo acids have much higher half-wave oxidation potentials than the alpha indole sulfo acids. A similar distinction was found to exist in the pyrrole sulfo acids.



(V)

We also had available a preparation of indolesulfonic-1 acid as its barium salt. We polarographed this sample as well in order to determine the effect of the N position of the sulfo group upon the oxidation potential.

Electrolytic oxidation of indolesulfonic-1 acid (VI). The barium salt of indolesulfonic-1 acid was oxidized smoothly at the mercury dropping electrode, yielding one wave with a half-wave oxidation potential of 0.025 volt (Fig. 6).

It is apparent from these findings that the magnitude of the oxidation potential is largely affected by the position of the sulfo group in the pyrrole ring. The beta indole sulfo acids have the highest potentials (i.e., are hardest to oxidize), while indolesulfonic-1 acid exhibits the lowest oxidation potential. Hence, the magnitude of the half-wave oxidation potential affords an indication of the position of the sulfo group in the indole molecule.

We felt it was also not without interest to make a study of the polarographic behavior of indole sulfo acids in which the sulfo group was not attached to the pyrrole ring.

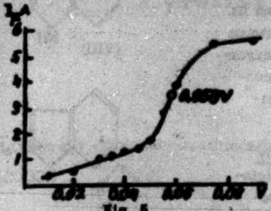


Fig. 5

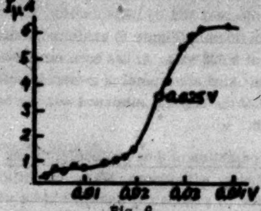


Fig. 6

We had available 2-methylindolesulfonic-5 acid, prepared by sulfonating 2-methylindole with oleum, and 3-indolylmethanesulfonic acid, prepared by methylenesulfonating indole. The position of the sulfo groups in the acids was rigorously established chemically.

Electrolytic oxidation of 2-methylindolesulfonic-5 acid (VII). The polarogram of the barium salt of 2-methylindolesulfonic-5 acid exhibits a single wave, with a half-wave potential of 0.020 volt (Figure 7).

Electrolytic oxidation of 3-indolylmethanesulfonic acid (VIII). The polarogram of 3-indolylmethanesulfonic acid closely resembles that of the preceding acid. Its half-wave oxidation potential was 0.018 volt (Figure 8).

We see that the half-wave oxidation potentials of both of these sulfo acids are very close together and appreciably lower than the potentials of the α- and β-indole sulfo acids. This indicates that a sulfo group that is not directly attached to a carbon atom in the pyrrole ring does not have much of an effect upon the stability of the indole molecule.

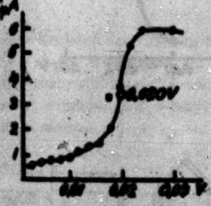


Fig. 7

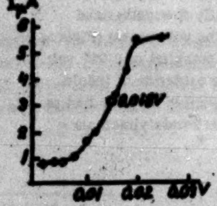


Fig. 8

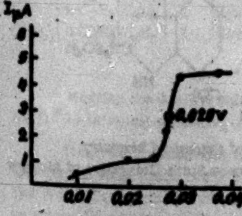


Fig. 9

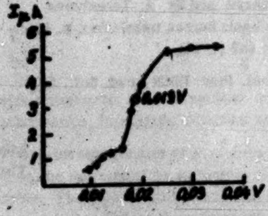
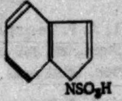
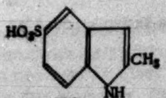


Fig. 10

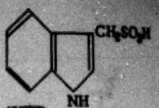


(VI)

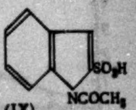


(VII)

On the basis of all these results we had secured, we employed the oxidation polarography method to solve the problem of the structure of several indole sulfo acids: 1-acetylindolesulfonic acid; 3-acetylindolesulfonic acid, prepared by sulfonating 3-acetylindole with oleum; and 2-methylindolesulfonic acid, prepared by sulfonating 2-methylindole with pyridine sulfotrioxide.



(VIII)



(IX)

Electrolytic oxidation of 1-acetylindolesulfonic acid (IX). The results of a chemical investigation of this acid have shown that it is most probable that the sulfo group enters this compound at the α- position. To resolve all doubts concerning the structure of the acid and its individuality, however, we polarographed its barium salt. The polarogram (Figure 9) exhibited a single wave with a halfwave oxidation potential of 0.028 volt. As has been established in the foregoing examples, potentials of this kind are typical of α- indole sulfo acids. It may be concluded, therefore, that the original substance was the barium salt of 1-acetylindolesulfonic-2 acid.

Electrolytic oxidation of 3-acetylindolesulfonic acid (X), prepared by sulfonating 3-acetylindole with oleum. When the barium salt of 3-acetylindolesulfonic acid, prepared by sulfonating 3-acetylindole with oleum, was polarographed, we found a single wave with a halfwave oxidation potential of 0.019 volt (Figure 10). This low potential indicates that the sulfo group is apparently not attached to the pyrrole ring. This is borne out by the results of oxidizing the salt with a chromic acid mixture, in which the sulfo group is not split off. By analogy the most probable structure of the original substance is: 3-acetylindolesulfonic-6 acid (it is in this position that 3-carbethoxyindole is nitrated and brominated).

Electrolytic oxidation of 2-methylindolesulfonic acid (XI), prepared by sulfonating 2-methylindole with pyridine sulfotrioxide. The properties of the methylindolesulfonic acid prepared by sulfonating 2-methylindole with pyridine sulfotrioxide (action on bromine water, hydrolysis by 15% HCl) differed from those of the α- and β-indole sulfo acids. The sulfo group was not attached to the benzene ring, however, as was proved by the results of oxidizing the barium salt with permanganate, the sulfo group being split off completely. Since we wanted to identify the synthesized acid more fully, we polarographed its barium salt. The polarogram (Figure 11) showed a single wave, with a halfwave oxidation potential of 0.017 volt. In the light of all our other results on the electrolytic oxidation of indole sulfo acids, in which the sulfo group was outside the pyrrole ring, we had to assume that the structure of the original substance was 2-indolylmethanesulfonic acid.

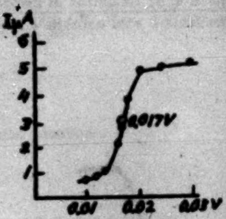
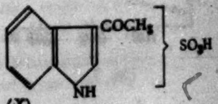
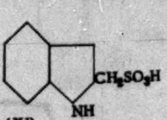


Fig. 11



(X)



(XI)

SUMMARY

It has been shown that the oxidative polarographic method may be employed to determine the position of the sulfo group in indole sulfo acids.

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Received September 29, 1950

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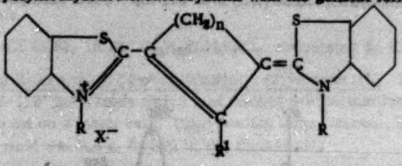
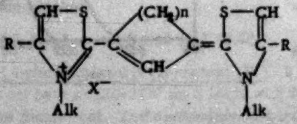
α, γ-POLYMETHYLENETHIAZOLECARBOCYANINS. I.

I. K. Ushenko

The α,γ-polymethylenethiacarbocyanins with the general formula:



(where R = CH_3, C_2H_5, C_6H_5; n = 0, 1, 2, 3, 4, 5, 6; R^1 = H, CH_3, C_2H_5) have been described by us previously [1,2]. The corresponding thiazolecarbocyanins:

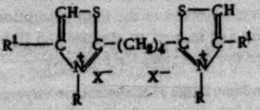


have not been described in the literature. We undertook to synthesize such dyes, containing a five-ring system (n = 2). For this purpose we synthesized two dithiazolylbutanes: α, ω-di-[4-methylthiazolyl-(2)]-butane [3] and α,ω-di[4-phenylthiazolyl-(2)]-butane [4]. These bases were heated in sealed tubes with dimethyl sulfate, and the methyl, ethyl, n-propyl, and n-butyl esters of p-toluenesulfonic acid. The ditertiary salts were isolated and purified in the usual manner.

TABLE 1

No.	R	R^1	X−	Melting point
(I)	CH_3	CH_3	ClO_4	278° (with decomposition)
(II)	C_2H_5	CH_3	ClO_4	268 "
(III)	CH_3	C_6H_5	I	272 "
(IV)	C_2H_5	C_6H_5	I	243 "
(V)	n-C_3H_7	C_6H_5	I	201 "
(VI)	n-C_4H_9	C_6H_5	I	212 "

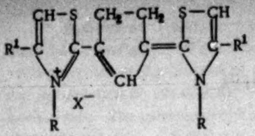
Small quantities of the alkyl p-toluenesulfonates were dissolved in hot water and converted into the corresponding dialkyl perchlorates and dialkyl iodides, listed in Table 1, by the action of an aqueous solution of sodium perchlorate or potassium iodide, respectively.



Heating the dialkyl sulfonates with orthoformic ester in pyridine or with acetic anhydride for a short interval (15-20 minutes) produced thiazolecarbocyanins, turning the solutions an intense blue.

It has been found that the dialkyl p-toluenesulfonates of α, ω-di-[4-phenylthiazoyl-(2)]-butane condense with orthoformic ester much more easily than do the corresponding sulfonates of α,ω-di-[4-methylthiazolyl-(2)]-butane. The synthesized dyes are extremely unstable. They are broken down completely when they stand for a long time in an alcoholic solution, or when attempts are made to isolate them from solution. As the dyes decompose, their solutions turn dark-green and red-purple. We have been able to determine the absorption maxima of these preparations despite their instability.

The absorption maxima of dyes with the general formula of:



in ethyl alcohol are listed in Table 2.

TABLE 2

No.	R	R^1	Absorption maxima (in mμ)
(VII)	C_2H_5	CH_3	595
(VIII)	C_2H_5	C_6H_5	596
(IX)	n-C_3H_7	C_6H_5	600
(X)	n-C_4H_9	C_6H_5	600

We know that unsubstituted 3,3'-diethylthiacarbocyanin iodide (XI) has an absorption maximum at 560 mμ. The λ_{max} of 3,3'-diethyl-8,10-dimethylthiacarbocyanin iodide (XII) is at 601 mμ . Their absorption curves are reproduced in Figure 1.

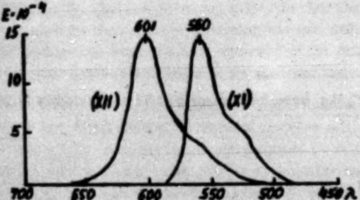


Fig. 1

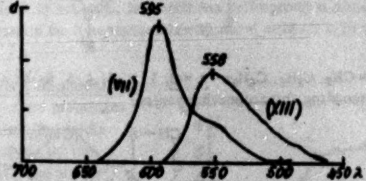


Fig. 2

Thus, closing the five-ring system in the thiacarbocyanins produces a bathochromic effect of 41 mμ .

3,3'-Diethyl-4,4'-dimethylthiazolecarbocyanin iodide (XIII) has an λ_{max} of 556 mμ . The 3,3'-diethyl-4,4'-dimethyl-6,8-dimethylenethiazolecarbocyanin (VII) we have synthesized has an absorption maximum at 595 mμ . The absorption curves of the last two preparations are given in Figure 2.

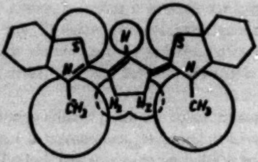


Fig. 3

In this case closing the five-ring system in the thiazolecarbocyanins produces about the same bathochromic effect. Now the question arises: what is responsible for this high stability of α, γ-dimethylenethiazolecarbocyanins? Apparently, closing the five-ring system sets up an obstacle to the coplanarity of the thiazole rings, which is reflected in the light absorption and in the stability of the dye. We had previously observed that color grew deeper and fastness to alkalies and light was diminished in 8,10-dimethylenethiacarbocyanin. The structure of this latter dye is pictured in Figure 3.

It is common knowledge that the thiazolecyanins are, in general, less stable than the thiacyanins [5]. It is not surprising that the introduction of a five-ring system into the thiazolecarbocyanin molecule diminishes the stability of the dye to such an extent that it cannot be recovered from solution.

EXPERIMENTAL*

α,ω-Di-[4-dimethylthiazolyl-(2)]-butane. This base was synthesized from the dithioamide of adipic acid and chloroacetone [3].

α,ω-Di-[4-phenylthiazolyl-(2)]-butane [4]. This was prepared from the dithioamide of adipic acid and bromoacetophenone [4].

Dimethylperchlorate of α,ω-di-[4-methylthiazolyl-(2)]-butane (I). 0.45 g of α,ω-di-[4-methylthiazolyl-(2)]-butane was heated on a boiling water bath for 1 hour with 0.45 g of dimethyl sulfate. The salt was very soluble in water. The reaction product was dissolved in a small quantity of water, boiled with activated charcoal, filtered, evaporated on a water bath, and thoroughly warmed to 137°. The yield totaled 0.85 g or 35% of the theoretical. 0.35 g of the methylmethyl sulfate was dissolved in a small quantity of water and converted by the action of sodium perchlorate into the dimethyl perchlorate of α-ωdi[4-methylthiazolyl-(2)]-butane. Its m.p. was 268° with decomposition after recrystallization from alcohol.

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* The experimental work was done in association with L. T. Belykh.

Found %: Cl 14.29, 14.30. $C_{14}H_{22}O_8S_2Cl_2$. Calculated %: Cl 14.76.

Diethyl perchlorate of α,ω-di-[4-methylthiazolyl-(2)]-butane (II.) 0.55 g of α,ω-di-[4-methylthiazolyl-(2)]-butane was heated with 0.8 g of ethyl p-toluenesulfonate for 6 hours in a sealed tube on an oil bath at 118-120°. The standard procedure was followed in the isolation and purification of the salt. A slightly yellowish solid. The yield was 1.8 g, or 81% of the theoretical. The diethyl perchlorate consisted of white crystals with a m.p. of 278° with decomposition.

Found %: Cl 13.85, 13.96. $C_{16}H_{26}O_8N_2S_2Cl_2$. Calculated %: Cl 13.90.

Dimethiodide of α,ω-di-[4-phenylthiazolyl-(2)]-butane (III). 2 g of the base was heated in a sealed tube on an oil bath at 115-118° for 4 hours with 2 g of methyl p-toluenesulfonate. The transparent aqueous solution of the salt was concentrated on a water bath. Upon cooling large, lustrous, light-greenish crystals, with a m.p. of 216°, settled out. The yield was 2.4 g, or 61% of the theoretical.

Found %: S 17.62, 17.76. $C_{38}H_{40}O_6N_2S_4$. Calculated %: S 17.12.

The dimethiodide of α,ω-di-[4-phenylthiazolyl-(2)]-butane consisted of light-yellow crystals, with a m.p. of 272° after recrystallization from alcohol.

Found %: I 38.07. $C_{24}H_{26}N_2S_2I_2$. Calculated %: I 38.63.

Diethiodide of α,ω-di-[4-phenylthiazolyl-(2)]-butane (IV). 2 g of α,ω-di-[4-phenylthiazolyl-(2)]-butane was heated in a sealed tube on an oil bath at 130-135° for 8 hours with 2 g of ethyl p-toluenesulfonate. The sulfonate yield was 2.15 g, or 52% of the theoretical. The diethiodide of α,ω-di-[4-phenylthiazolyl-(2)]-butane consisted of lustrous crystals, m.p. 243° with decomposition.

Found %: I 36.83, 36.65. $C_{26}H_{30}S_2N_2I_2$. Calculated %: I 36.93.

Di-n-propiodide of α,ω-di-[4-phenylthiazolyl-(2)]-butane (V). 1.2 g of α,ω-di-[4-phenylthiazolyl-(2)]-butane (1 mole) was heated in a sealed tube on an oil bath at 140° for 12 hours with 1.3 g of n-propyl p-toluenesulfonate (2 moles). The yield was 0.25 g, or 34% of the theoretical. White crystals that turned yellow upon standing.

Di-n-butiodide of α,ω-di-[4-phenylthiazolyl-(2)]-butane (VI). 1.2 g of the base was heated with 1.4 g of n-butyl p-toluenesulfonate to 140° for 12 hours. The yield was 0.25 g, or 10% of the theoretical. Recrystallization from a 1:1 water-alcohol mixture yielded the di-n-butiodide as colorless crystals with a m.p. of 212°.

Found %: I 34.24. $C_{30}H_{38}N_2S_2I_2$. Calculated %: I 34.16.

DYES

3,3'-Diethyl-4,4'-dimethyl-6,8-dimethylenethiazolecarbocyanin p-toluenesulfonate (VII). 0.3 g of the di-(ethyl p-sulfonate) of α,ω-di-[4-methylthiazolyl-(2)]-butane was boiled for 20 minutes with 0.3 g of ethyl orthoformate and 2.5 ml of pyridine. The solution turned deep blue. We were unable to isolate the dye in the pure state, since it decomposed quickly. Its absorption maximum lay at 595 mμ.

3,3'-Diethyl-4,4'-diphenyl-6,8-dimethylenethiazolecarbocyanin p-toluenesulfonate (VIII). 1.5 g of the di-(ethyl p-sulfonate) of α,ω-di-[4-phenylthiazolyl-(2)]-butane was boiled with 1.5 g of ethyl orthoformate and 2 ml of pyridine for 20 minutes. The solution turned deep blue. The dye decomposed quickly. The absorption maximum lay at 596 mμ.

3,3'-Di-n-propyl-4,4'-diphenyl-6,8-dimethylenethiazolecarbocyanin p-toluenesulfonate (IX). 0.5 g of the di-(n-propyl p-toluenesulfonate) of α,ω-di-[4-phenylthiazolyl-(2)]-butane was boiled for 20 minutes with 0.5 g of ethyl orthoformate, and 2 ml of pyridine. A deep blue color appeared very quickly. The dye was unstable, and we were unable to secure it in the pure state. The absorption maximum lay at 600 mμ.

3,3'-Di-n-butyl-4,4'-diphenyl-6,8-dimethylenethiazolecarbocyanin p-toluenesulfonate (X). 0.1 g of the di-(n-butyl p-toluenesulfonate) of α,ω-di-[4-phenylthiazolyl-(2)]-butane and 0.1 g of ethyl orthoformate were boiled in 2 ml of pyridine to which 2-3 drops of acetic anhydride had been added. We were unable to isolate the dye in the pure state. Its absorption maximum lay at 600 mμ.

The author is deeply indebted to Prof. A. I. Kiprianov for his valuable counsel.

SUMMARY

1. Six new ditertiary salts have been synthesized by heating α,ω-di-[4-methylthiazolyl-(2)]-butane and α,ω-di-[4-phenylthiazolyl-(2)]-butane with dimethyl sulfate and the methyl, ethyl, n-propyl, and n-butyl esters of p-toluenesulfonic acid.

2. The dialkyl p-toluenesulfonates were condensed with ethyl orthoformate in pyridine or acetic anhydride; this yielded unstable α,γ-dimethylenethiazolecarbocyanins, which could hot be recovered from their solutions. Their absorption maxima in ethyl alcohol have been determined.

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Received July 18, 1950

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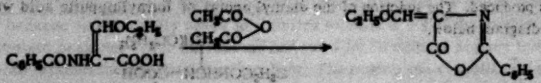
THE REACTION OF THE DIETHYL ACETAL OF FORMYLHIPPURIC ACID WITH THIONYL CHLORIDE

A. S. Elina and O. Yu. Magidson

Study of complex molecules that contain diverse functional groups is of special interest, since it establishes the sensitivity of the individual functional groups to any reagent. The diethyl acetal of formylhippuric acid is a complex molecule of that type. We have investigated the reaction of the diethyl acetal of formylhippuric acid with thionyl chloride.

When the diethyl acetal of formylhippuric acid was reacted with thionyl chloride in a benzene solution (the benzene being absolutely anhydrous and the molar ratio being 1:1), we obtained a compound that contained no chlorine and might be taken to be ethoxymethylenehippuric acid, on the basis of its analysis. This was established by securing 2-phenyl-4-ethoxymethyleneoxazolinone-(5) when the substance was heated with acetic anhydride:

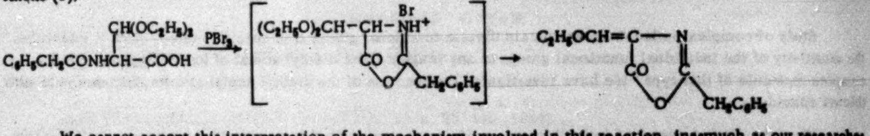


In contrast to the ethoxymethylene group in 2-phenyl-4-ethoxyoxazolinone-(5), the ethoxymethylene group in ethoxymethylenehippuric acid is highly alkali-resistant; it cannot be saponified, not only in the mild conditions employed to saponify the analogous group in 2-phenyl-4-ethoxymethyleneoxazolinone-(5), but not even when heated with an alkali.

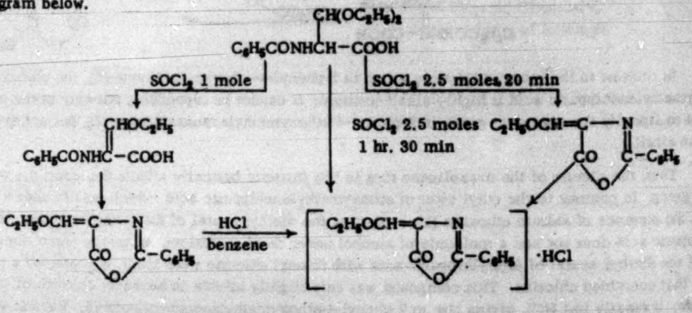
Thus, the closure of the oxazolinone ring in this instance basically affects the reactivity of the ethoxymethylene group. In contrast to the ethyl ester of ethoxymethylenehippuric acid, which readily adds a molecule of alcohol in the presence of sodium ethoxide [1], producing the diethyl acetal of the formylhippurate, the ethoxymethylenehippuric acid does not add a molecule of alcohol under these conditions. When the proportions used in the reaction of the diethyl acetal of formylhippuric acid with thionyl chloride were 1:2.5, we obtained a crystalline compound that contained chlorine. This compound was very slightly soluble in benzene, chloroform, and carbon tetrachloride; it readily lost HCl, giving rise to 2-phenyl-4-ethoxymethyleneoxazolinone-(5), when it was heated in these solvents, when it was stored with the air excluded, and when it was treated with a $NaHCO_3$ solution or even with water. When a current of anhydrous HCl was passed through a chilled solution of 2-phenyl-4-ethoxymethyleneoxazolinone-(5) in absolute benzene, we obtained its hydrochloride, whose crystalline form and properties were the same as those of the chlorine-containing compound we had secured by reacting 1 part of the diethylacetal of formylhippuric acid with 2.5 parts of thionyl chloride as described above. All these findings led us to conclude that when the diethyl acetal of formylhippuric acid is reacted with an excess of thionyl chloride (1:2.5), ethoxymethylenehippuric acid is first produced, after which the oxazolinone ring is closed and the hydrochloride of 2-phenyl-4-ethoxymethyleneoxazolinone-(5) is formed. The closure of the oxazolinone ring may precede the stage in which the ethoxymethylenehippuryl chloride is formed; but if this compound exists, it is so unstable that it cannot be isolated. Our conclusions were further borne out by the fact that 2-phenyl-4-ethoxymethyleneoxazolinone-(5) was produced when equal parts of ethoxymethylenehippuric acid and thionyl chloride were reacted together. Moreover, when we interrupted the reaction of the diethyl acetal of formylhippuric acid with an excess of thionyl chloride (1:2.5 ratio) long before the crystalline hydrochloride of 2-phenyl-4-ethoxymethyleneoxazolinone-(5) began to settle out of the benzene solution and then drove off the benzene in vacuo without applying any heat, we secured a nearly quantitative yield of 2-phenyl-4-ethoxymethyleneoxazolinone-(5).

It is worthy of note that 2-phenyl-4-anilinomethyleneoxazolinone, whose m.p. was 164-165°, was produced by reacting the hydrochloride of 2-phenyl-4-ethoxymethyleneoxazolinone-(5), synthesized from the diethyl acetal of formylhippuric acid, with aniline, whereas the 2-phenyl-4-anilinomethyleneoxazolinone prepared from 2-phenyl-4-ethoxymethyleneoxazolinone-(5) had a m.p. of 154-155° after repeated recrystallization from alcohol, which is the melting point given in the literature [2]. The mixed melting point of these two anilinomethyleneoxazolinones exhibited no depression. When the low-melting 2-phenyl-4-anilinomethyleneoxazolinone-(5) was recrystallized from alcohol to which a small quantity of the high-melting anilinomethyleneoxazolinone had been added, the low-melting anilinomethylene derivative was converted nearly quantitatively into the high-melting one with a m.p. of 164-165°.

The recently published monograph "The Chemistry of Penicillin" [3] states that the action of PBr_3 upon the diethyl acetal of α-formylphenaceturic acid yields the hydrobromide of 2-benzyl-4-ethoxymethyleneoxazolinone-(5). The authors believe the following to be the probable reaction mechanism involved: at first, the hydrobromide of 2-benzyl-4-diethoxymethyloxazolinone-(5) is formed, but it cannot be isolated because of its extreme instability, and it gives up a molecule of ethyl alcohol and is converted into the hydrobromide of 2-benzyl-4-ethoxymethyleneoxazolinone-(5):



We cannot accept this interpretation of the mechanism involved in this reaction, inasmuch as our researches (cited above) on a nearly analogous reaction, namely, the reaction of the diethyl acetal of formylhippuric acid with thionyl chloride, have shown that a molecule of ethyl alcohol is first split off, yielding ethoxymethylenehippuric acid, after which the ring is closed, forming 2-phenyl-4-ethoxymethyleneoxazolinone-(5), and finally, the latter's hydrochloride is produced. The reaction of the diethyl acetal of formylhippuric acid with thionyl chloride may be pictured by the diagram below.



EXPERIMENTAL

Ethoxymethylenehippuric acid. A solution of 0.85 g of the diethyl acetal of formylhippuric acid in 5.5 ml of absolute benzene was chilled while a solution of 0.37 g of $SOCl_2$ (1 mole per mole) in 3 ml of absolute benzene was slowly added. After the mixture had stood for 30-40 minutes at room temperature, the benzene was driven off in vacuo without the application of any heat. The residue, a brittle solid mass, was processed with a small amount of dichloroethane, the precipitated ethoxymethylenehippuric acid being filtered out. Another 0.1 g of ethoxymethylenehippuric acid was recovered from the mother liquor. Total yield was 0.5 g, or 70.4% of the theoretical.

After crystallization from dichloroethane the ethoxymethylenehippuric acid was a colorless crystalline substance with a m.p. of 187-188°, soluble when heated in water, but insoluble in ether.

7.599 mg substance: 0.392 ml N_2 (18°, 730.5 mm). 6.782 mg substance: 8.66 ml 0.02 N $Na_2S_2O_3$. Found %: N 5.82; OC_2H_5 19.17. $C_{12}H_{13}O_4N$. Calculated %: N 5.95; OC_2H_5 19.13.

Action of an alkali upon ethoxymethylenehippuric acid. a) A solution of 0.1 g of ethoxymethylenehippuric acid in 3 ml of 5% NaOH was allowed to stand for 4 hours at room temperature, after which it was acidulated until its reaction was acid with Congo red. A total of 0.09 g of the unchanged ethoxymethylenehippuric acid was recovered.

b) A solution of 0.1 g of ethoxymethylenehippuric acid in 4 ml of 5% NaOH was heated to 70-75° for 3 hours and then allowed to stand for 12 hours at room temperature. When the solution was acidulated, the ethoxymethylenehippuric acid was precipitated unchanged.

Action of absolute alcohol and sodium ethoxide upon ethoxymethylenehippuric acid. 0.27 g of ethoxymethylenehippuric acid was added to a solution of 0.03 g of Na in 5 ml of absolute alcohol, the solution was heated to

60-65° for two hours and set aside to stand at room temperature for 18 hours. The alcohol was driven off in vacuo, the residue dissolved in water, and the solution filtered and acidulated. The crystalline precipitate was filtered out, washed with water, and dried (0.24 g), m.p. 182-184°. The melting point of the substance rose to 188-189° after crystallization from water. The mixed melting point with ethoxymethylenehippuric acid exhibited no depression.

Synthesis of 2-phenyl-4-ethoxymethyleneoxazolinone-(5) from ethoxymethylenehippuric acid. a) 0.3 g of ethoxymethylenehippuric acid was heated in 2 ml of acetic anhydride for 20 minutes on a water bath. The reaction solution was poured into water and processed with diethyl ether. The ether extract was treated a few times with a solution of $NaHCO_3$ and then with water, and dried with anhydrous Na_2SO_4, after which the ether was driven off. The residue, a crystalline substance (0.25 g), was recrystallized from petroleum ether. Recrystallization yielded a nearly colorless crystalline substance (needles) with a m.p. of 95-96°. The mixed melting point with 2-phenyl-4-ethoxymethyleneoxazolinone-(5) exhibited no depression.

b) 0.1 g of $SOCl_2$ in 2 ml of chloroform was gradually added to a chilled mixture of 0.21 g of ethoxymethylenehippuric acid and 7 ml of anhydrous chloroform. The ethoxymethylenehippuric acid slowly dissolved after the mixture had stood for 2 hours. The chloroform was driven off in vacuo at room temperature, leaving a residue of 0.19 g, which was dissolved in absolute benzene. The benzene was driven off until the residual volume was small, and petroleum ether was added as soon as crystals began to settle out. The precipitated crystalline substance was filtered out. Needles with a m.p. of 94-96°. The mixed melting point with 2-phenyl-4-ethoxymethyleneoxazolinone-(5) exhibited no depression.

Reaction of 1 mole of the diethyl acetal of formylhippuric acid with 2.5 moles of thionyl chloride. a) 1.1 g of $SOCl_2$ in 2 ml of absolute benzene was gradually added to a chilled solution of 1 g of the diethyl acetal of formylhippuric acid in 6 ml of absolute benzene. After the mixture had stood for 20 minutes at room temperature, the benzene was driven off in vacuo without the application of any heat. The residue was crystallized from petroleum ether, yielding a crystalline substance with a m.p. of 93-95°, which possessed all the properties of 2-phenyl-4-ethoxymethyleneoxazolinone-(5). Recrystallization from petroleum ether yielded nearly colorless needles with a m.p. of 95-96°, whose mixed melting point with 2-phenyl-4-ethoxymethyleneoxazolinone-(5) exhibited no depression.

b) 1.1 g of $SOCl_2$ in 2 ml of absolute benzene was gradually added to a chilled solution of 1 g of the diethyl acetal of formylhippuric acid in 6 ml of absolute benzene. After the mixture had stood for 1.5 hours at room temperature, the nearly colorless crystalline precipitate of the hydrochloride of 2-phenyl-4-ethoxymethyleneoxazolinone-(5), weighing 0.6 g, was filtered out. It was thoroughly washed free of the reaction solution by repeatedly mixing it with absolute benzene, filtering it out, and rewashing it on the filter.[*] 2-Phenyl-4-ethoxymethyleneoxazolinone-(5) hydrochloride is insoluble in ether, benzene, dichloroethane, chloroform, or carbon tetrachloride; it decomposes upon standing, giving off HCl and yielding 2-phenyl-4-ethoxymethyleneoxazolinone-(5). A quantitative yield of 2-phenyl-4-ethoxymethyleneoxazolinone-(5) was produced when the 2-phenyl-4-ethoxymethyleneoxazolinone-(5) was treated with a $NaHCO_3$ solution or with water. 2-Phenyl-4-ethoxymethyleneoxazolinone-(5) hydrochloride does not have a sharp melting point, fusing between 90 and 94°. The 2-phenyl-4-ethoxymethyleneoxazolinone-(5) hydrochloride apparently breaks down in the capillary, yielding 2-phenyl-4-ethoxymethyleneoxazolinone-(5).

8.394 mg substance: 4.415 mg AgCl. Found %: Cl 13.01. $C_{12}H_{11}O_3N \cdot HCl$. Calculated %: Cl 13.98.

2-Phenyl-4-ethoxymethyleneoxazolinone-(5) hydrochloride from 2-phenyl-4-ethoxymethyleneoxazolinone-(5). A current of dry HCl was passed through a chilled solution of 1.5 g of 2-phenyl-4-ethoxymethyleneoxazolinone-(5) in 15 ml of absolute benzene for 5 minutes. Crystals of 2-phenyl-4-ethoxymethyleneoxazolinone-(5) hydrochloride begin to settle out as soon as the passage of the HCl is initiated. The 2-phenyl-4-ethoxymethyleneoxazolinone-(5) hydrochloride was filtered out and processed repeatedly with absolute benzene, after which it was a nearly colorless crystalline substance that was insoluble in ether, benzene, chloroform, dichloroethane, or carbon tetrachloride. All the other properties of this substance were the same as those of the 2-phenyl-4-ethoxymethyleneoxazolinone hydrochloride prepared from the diethyl acetal of formylhippuric acid, m.p. 90-94°.

High-melting 2-phenyl-4-anilinomethyleneoxazolinone-(5). 0.15 g of aniline was added to 0.2 g of 2-phenyl-4-ethoxymethyleneoxazolinone-(5) in 2 ml of absolute $CHCl_3$. The initial substance dissolved gradually, a colorless crystalline precipitate – aniline hydrochloride – being thrown down. The aniline hydrochloride (0.1 g) was filtered out. The solution was evaporated, and the 0.8 g of yellow crystalline precipitate was crystallized a few times from ethyl alcohol. 2-Phenyl-4-anilinomethyleneoxazolinone-(5) consisted of yellow needles with a m.p. of 164-165°.

5.564 mg substance: 0.519 ml N_2 (20.5° at 743 mm). Found %: N 10.6. $C_{16}H_{12}O_2N_2$. Calc.%: N 10.61.

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[*] 0.2 g of 2-phenyl-4-ethoxymethyleneoxazolinone-(5) was recovered from the benzene mother liquor after the benzene had been driven off.

2-Phenyl-4-anilinomethyleneoxazolinone-(5) from 2-phenyl-4-ethoxymethyleneoxazolinone-(5). 0.33 g of aniline was added to a solution of 0.35 g of 2-phenyl-4-ethoxymethyleneoxazolinone-(5) in 3 ml of ethyl alcohol. A yellow crystalline precipitate began to settle out at once; after the mixture had stood for a few minutes, the precipitate (0.41 g) was filtered out and crystallized from ethyl alcohol. The m.p. of 2-phenyl-4-anilinomethyleneoxazolinone-(5) (yellow needles) was 154-155° after four crystallizations from ethyl alcohol. The mixed melting point with the high-melting 2-phenyl-4-anilinomethyleneoxazolinone-(5) was 164-165°.

The 2-phenyl-4-anilinomethyleneoxazolinone-(5) with a m.p. of 154-155° was recrystallized from ethyl alcohol to which a small amount of the high-melting 2-phenyl-4-anilinomethyleneoxazolinone-(5) had been added. The anilinomethylene derivative secured after this crystallization had a m.p. of 164-165°.

SUMMARY

1. It has been found that when equal molar proportions of the diethyl acetal of formylhippuric acid and thionyl chloride are reacted together, a molecule of ethyl alcohol is split out and ethoxymethylenehippuric acid is formed, which reacts with acetic anhydride or thionyl chloride (1 mole: 1 mole) to yield 2-phenyl-4-ethoxymethyleneoxazolinone-(5).

2. It has been proved that the ethoxymethylene group in ethoxymethylenehippuric acid differs from the analogous group in 2-phenyl-4-ethoxymethyleneoxazolinone-(5) in resisting the action of an alkali.

3. It has been established that when 1 mole of the diethyl acetal of formylhippuric acid is reacted with 2.5 moles of thionyl chloride, 2-phenyl-4-ethoxymethyleneoxazolinone-(5) is formed, while prolonged interaction yields the hydrochloride of 2-phenyl-4-ethoxymethyleneoxazolinone-(5).

4. The reaction mechanism proposed by the American authors Hunter, Hinman, and Carter for the formation of salts of 2-phenyl-4-alkoxymethyleneoxazolinones is utterly unfounded.

5. It has been established that 2-phenyl-4-anilinomethyleneoxazolinone-(5) exists in two forms: the low-melting (154-155°) and the high-melting (164-165°), and the conversion of the low-melting form into the high-melting one has been effected.

LITERATURE CITED

[1] A. Ya. Berlin, V. I. Maimind, and E. S. Golombik. J. Gen. Chem., 21, 132 (1951); see Consultants Bureau translation, p. 145.

[2] British Patent 585089; Chem. Abs., 41, 3822 (1947).

[3] Y.H.Hunter, Y.W.Hinman and H.E.Carter. The Chemistry of Penicillin (1949), Chap. XXIV, pp. 911, 915, 916.

Received September 20, 1950

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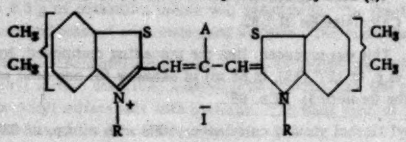
RESEARCHES ON CYANIN DYES

VII. THE PROPERTIES OF TETRAMETHYLTHIACARBOCYANINS

I.I. Levkoev, A.F. Vompe, N.N. Sveshnikov, and N.S. Barvin

In several symmetrical thiacarbocyanins, the entrance of electron donor groups at the 5,5' and 6,6' positions shifts the absorption maximum of the dyes appreciably toward the longer wavelengths, whereas the presence of the same groups at the 4,4' or 7,7' position deepens the color of the dye only slightly [1-6]. We were interested in ascertaining the effect of the entrance of two identical or dissimilar electron donor groups at different positions in the heterocyclic rings upon the optical and photographic properties of the thiacarbocyanins. It was advisable to begin with a study of the symmetrical dyes of this class, which contain 4 identical substituent groups in various positions on the heterocyclic rings. In the present research, we have synthesized and investigated several 4,5,4',5'-, 4,6,4',6'-, 4,7,4',7'-, 5,6,5',6'-, 5,7,5'7'- and 6,7,6',7'-tetramethylthiacarbocyanins (I).



A = H or CH_3 ($R = C_2H_5$) or
A = C_2H_5 ($R = CH_3$ or C_2H_5)

(I)

Of all these dyes, only a few 5,6,5',6',-derivatives are cited in one of the patents [7], being suggested as sensitizers for silver halide emulsions. According to this patent, the entrance of methyl groups at the 5,6,5',6', positions in thiacarbocyanins produces a fairly substantial bathochromic shift of the absorption maximum.

We synthesized the initial 2,4,5-, 2,4,7- and 2,5,7-trimethylbenzothiazoles, as well as the 2,4,6-trimethylbenzothiazole described previously [8], by oxidizing the thioacetyl derivatives of the respective aminoxylenes with potassium ferricyanide (see [9]). The 2,5,6- and 2,6,7-trimethylbenzothiazoles were synthesized by heating the respective 2-aminodimethylbenzothiazoles with potassium hydroxide and processing the resulting salts of aminothioxylenes with acetic anhydride [10].

TABLE 1

Location of the Absorption Maxima of the Ethylates of Di- and Tetramethylcarbocyanins (In Ethyl Alcohol)

Location of methyl groups	Location of absorption maxima (in mμ)		
	Substituents at the 9 position		
	H	CH_3	C_2H_5
–	557	543	547
4,4'-[1][a]	563	547	–
5,5'-	565	548	550
6,6'-	563	548	552
4,5,4',5'-	568	550	553
4,6,4',6'-	568	552	556
4,7,4',7'-	566	550	554
5,6,5',6'-	570	554	558
5,7,5',7'-	568	553	557
6,7,6',7'-	568	553	557

Most of the dyes were synthesized by heating the reactive alkyl p-toluenesulfonates of the isomeric trimethylbenzothiazoles with ortho esters of carboxylic acids in pyridine [11] and were isolated as well-crystallized iodides. Inasmuch as the yields of the alkyl p-toluenesulfonates of the 2,4,5-trimethylbenzothiazoles are low when produced under ordinary conditions, we employed the respective alkylalkyl sulfates, previously isolated in the pure state, in synthesizing the dyes.

The absorption maxima of the ethylates of the synthesized tetramethylthiacarbocyanins and of some dimethyl derivatives are listed in Table 1.

We see from the table that the color is deepened whenever a dimethylthiacarbocyanin is converted into a tetramethylthiacarbocyanin. The

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[a] Footnote [1] refers to the 4,4-dimethylthiacarbocyanins, since the cited values of the absorption maxima for these dyes were taken from the paper cited.

5,6,5',6'-tetramethyl derivative exhibits the greatest shift of the absorption maximum toward the longer wave-lengths, as compared to the unsubstituted dye, while the least deepening of color is exhibited by the 4,7,4',7' substitution derivative of the dye. Hence, the second substituent group produces a greater shift of the absorption maximum toward the longer wave-lengths in tetramethylthiacarbocyanins when it enters at the 5,5' and 6,6' positions.

The tetramethylthiacarbocyanins are sensitizers of average efficiency. The ability of the corresponding 9-alkyl derivatives to act as second-order sensitizers is rather slight, being somewhat greater in the 5,6,5',6' substitution derivatives.

EXPERIMENTAL

(Together with A. G. Guseva and N. S. Stokovskaya)

Synthesis of Intermediates

3-Thioacetamino-1,2-xylene. 3.35 g of pulverized phosphorus pentasulfide was gradually added to a boiling solution of 8.15 g of 3-acetamino-1,2-xylene with a m.p. of 134-135° [12] in 35 ml of anhydrous benzene, and the mixture was then boiled for 30 minutes. The benzene solution was decanted from the tarry mass, which was washed with 75 ml of benzene. The benzene solutions were combined and then agitated with a 4% sodium hydroxide solution (three times, using 50-ml portions). The alkaline solution was neutralized with acetic acid and by passing carbon dioxide through. The 3-thioacetamino-1,2-xylene was recovered as a colorless crystalline precipitate. The yield was 5.0 g (62.5% of the theoretical). M.p. 130-131°.

Colorless prisms with a m.p. of 134-135°, after 3 recrystallizations from 50% ethyl alcohol.

Found %: N 7.75. $C_{10}H_{13}NS$. Calculated %: N 7.82.

4-Thioacetamino-1,3-xylene. This was produced like the preceding compound, by boiling a solution of 10 g of 4-acetamino-1,3-xylene, with a m.p. of 127° [13], in 60 ml of benzene for one hour with 4.08 g of phosphorus pentasulfide. The yield was 60% of the theoretical. M.p. 68°.

Crystallization from 50% ethyl alcohol yielded colorless crystals with a m.p. of 93° (Jacobson and Ney [8] give the m.p. as 94-95°).

5-Thioacetamino-1,3-xylene. A mixture of 4.37 g of 5-acetoamino-1,3-xylene, with a m.p. of 142° (Wroblewsky [14] gives the m.p. of 144.33°, while Noelting and Forel [12] give it as 140.5°), and 1.78 g of phosphorus pentachloride was added to 30 ml of boiling anhydrous benzene during the course of 1 hour, after which the liquid was refluxed for 2 hours. The product was isolated in the same way as was the 3-thioacetamino-1,3-xylene. The yield was 2.87 g (59.8% of the theoretical). M.p. 91-92°. Nearly colorless crystals with a m.p. of 93° (from ethyl alcohol).

Found %: N 7.95, 7.67. $C_{10}H_{13}NS$. Calculated %: N 7.82.

2-Thioacetamino-1,4-xylene. This was prepared, like the preceding compound, by reacting 5.4 g of 2-acetamino-1,4-xylene, with a m.p. of 137-138° (Schaumann [15] gives the m.p. as 138-139°, while Noelting, Witt, and Forel [16] give 139°), with 2.2 g of phosphorus pentasulfide in 35 ml of boiling benzene. The yield was 56.5% of the theoretical. Colorless crystals (from ethyl alcohol), m.p. 76°.

Found %: N 7.81. $C_{10}H_{13}NS$. Calculated %: N 7.82.

2,4,5-Trimethylbenzothiazole. A solution of 3.58 g of 3-thioacetamino-1,2-xylene (with a m.p. of 130-131°) in 80 ml of 4% potassium hydroxide was gradually added, with vigorous stirring, at 3-5° to a solution of 13.2 g of potassium ferricyanide in 55 ml of water. The mixture was stirred for 2 hours, after which the precipitate was extracted with ether, the ether driven off, and the residue distilled with steam. The distillate was extracted with ether, the extract dried with potash, and the ether driven off, the residue turning into a colorless crystalline mass when chilled. The yield was 2.80 g (79% of the theoretical). M.p. 50-51°.

The base was secured as colorless prisms with a m.p. of 54-55° after distillation in vacuo (b.p. 149-150° at 19 mm) and triple crystallization from gasoline.

Found %: N 7.78. $C_{10}H_{11}NS$. Calculated %: N 7.91.

Picrate. Large yellow prisms (from ethyl alcohol). M.p. 142-143°.

Found %: N 13.68. $C_{16}H_{14}O_7N_4S$. Calculated %: N 13.79.

Methylmethyl sulfate. This was prepared by heating 1.06 g of 2,4,5-trimethylbenzothiazole with 0.78 g of dimethyl sulfate on a boiling water bath for 3 hours. The crystallized mass was washed with ether and acetone. The yield was 1.55 g (83% of the theoretical).

Minute colorless prisms (from acetone), m.p. 213-215° (with decomposition).

Found %: N 4.60. $C_{12}H_{17}O_4NS_2$. Calculated %: N 4.61.

Methiodide. An 81.2% yield of this derivative was secured by adding potassium iodide to an aqueous solution of the preceding compound.

Colorless prisms (from ethyl alcohol), m.p. 215-216°.

Found %: N 4.42. $C_{11}H_{14}NSI$. Calculated %: N 4.38.

Ethylethyl sulfate. A mixture of 1.06 g of 2,4,5-trimethylbenzothiazole and 0.87 g of diethyl sulfate was heated to 130° for 5 hours. The crystalline mass was washed with anhydrous ether and triturated with 3 ml of anhydrous acetone. The precipitate was filtered out and washed with 2 ml of acetone. The yield was 0.35 g. M.p. 208-209°. Colorless prisms (from acetone), m.p. 215-217°. Very freely soluble in ethyl alcohol and in water.

Found %: N 4.32. $C_{14}H_{21}O_4NS_2$. Calculated %: N 4.20.

The acetone mother liquor and the wash liquid, which contained the ethyl sulfate salt of the base, were evaporated to dryness, the residue being dissolved in 10 ml of water, and 0.5 g of pyridine added to it.

The resultant bases were extracted with ether, and the aqueous solution was evaporated until its volume totaled 3 ml, after which 0.5 g of potassium iodide was added to it. The precipitated 2,4,5-trimethylbenzothiazole methiodide was filtered out and washed with water and acetone. The yield was 0.18 g. M.p. 204-205°.

0.35 g of 2,4,5-trimethylbenzothiazole, with a m.p. of 51-52°, was recovered from the ether solution of the wash water of the ethylethyl sulfate reaction. Another 0.20 g of the base was isolated from the ether solution produced by decomposing the ethyl sulfate salt with pyridine. The total yield of the quaternary salt was 26% of the theoretical, or 55% on the basis of the reacted base.

Ethiodide. Slightly grayish needles (from ethyl alcohol). M.p. 205-206°.

Found %: N 4.33. $C_{12}H_{16}NSI$. Calculated %: N 4.20.

2,4,6-Trimethylbenzothiazole. This was synthesized, like the preceding base, by adding 5.37 g of 4-thioacetamino-1,3-xylene in 120 mo of 4% sodium hydroxide to a solution of 20.6 g of potassium ferricyanide in 80 ml of water. The next day the liquid was extracted with ether, the extract dried with potash, the ether driven off, and the residue distilled in vacuo. A fraction with a b.p. of 146-148° at 15 mm was collected. The yield was 56.5% of the theoretical (when Jacobson and Nay [8] synthesized 2,4,6-trimethylbenzothiazole, their yield was 32%). Slightly yellowish oil.

Picrate. Yellow prisms with a m.p. of 138-139° (after double recrystallization from ethyl alcohol).

2,4,7-Trimethylbenzothiazole. This was synthesized, like the preceding base, by oxidizing 2-thioacetamino-1,4-xylene with potassium ferricyanide. The residue crystallized completely after the ether had been driven off. The yield was 97% of the theoretical. M.p. 29°. The base was purified by distilling it in vacuo. B.p. 132-133° at 9 mm. Colorless acicular crystals, m.p. 29°.

Found %: N 7.95. $C_{10}H_{11}NS$. Calculated %: N 7.91.

Picrate. Large light-yellow prisms (from ethyl alcohol). M.p. 142°.

Found %: N 13.90, 13.84. $C_{16}H_{14}O_7N_4S$. Calculated %: N 13.79.

2,5,7-Trimethylbenzothiazole. A filtered solution of 2.52 g of 5-thioacetamino-1,3-xylene in 60 ml of 4% potassium hydroxide was gradually added, with vigorous stirring, during the course of one hour to a solution of 9.65 g of potassium ferricyanide in 35 ml of water, chilled to 3-5°. A gray crystalline precipitate was thrown down. After two hours of stirring, the precipitate was filtered out, washed with water, and dried. The yield was 2.3 g (92% of the theoretical). M.p. 79-80°. The base was purified by crystallizing it twice from gasoline. Colorless prisms with a m.p. of 84°.

Found %: N 7.99, 8.02. $C_{10}H_{11}NS$. Calculated %: N 7.91.

Picrate. Yellow needles (from ethyl alcohol). M.p. 176°.

TABLE 2

Name of dye	Base, g	p-Toluenesulfonate, g	Ortho ester and its quantity, g	Ml of pyridine	% of theoretical yield
3,3'-Diethyl-4,6,4',6'-tetramethylthiacarbocyanin iodide	0.18	0.22	I–0.30	1.0	29
3,3'-Diethyl-4,6,4',6',9'-pentamethylthiacarbocyanin iodide	0.53	0.66	II–1.46*	3.0	22
3,3'9-Triethyl-4,6,4',6'-tetramethylthiacarbocyanin iodide	0.53	0.66	III–0.79**	3.0	14
3,4,6,3',4',6'-Hexamethyl-9-ethylthiacarbocyanin iodide	0.18	0.20	III–0.26	1.0	22
3,3'-Diethyl-4,7,4',7'-tetramethylthiacarbocyanin iodide	0.18	0.22	I–0.30	1.0	26
3,3'-Diethyl-4,7,4',7',9-pentamethylthiacarbocyanin iodide	0.53	0.66	II–1.46*	3.0	15
3,3',9-Triethyl-4,7,4',7' -tetramethylthiacarbocyanin iodide	0.53	0.66	III–0.79**	3.0	13
3,3'-Diethyl-5,6,5',6'-tetramethylthiacarbocyanin iodide	0.18	0.22	I–0.30	1.0	95
3,3'-Diethyl-5,6,5',6',9-pentamethylthiacarbocyanin iodide	0.53	0.66	II–0.97	3.0	53.5
3,3',9-Triethyl-5,6,5',6'-tetramethylthiacarbocyanin iodide	0.53	0.66	III–0.79	2.0	63
3,5,6,3',5',6'-Hexamethyl-9-ethylthiacarbocyanin iodide	0.71	0.82	III–1.06	4.0	63
3,3'-Diethyl-5,7,5',7',-tetramethylthiacarbocyanin iodide	0.18	0.22	I–0.30	1.0	55
3,3'-Diethyl-5,7,5',7',9-pentamethylthiacarbocyanin iodide	0.53	0.66	II–1.46	3.0	23
3,3',9-Triethyl-5,7,5',7'-tetramethylthiacarbocyanin iodide	0.53	9.66	III–0.79	3.0	12
3,5,7,3',5',7'-Hexamethyl-9-ethylthiacarbocyanin iodide	0.18	0.22	III–0.26	1.0	55
3,3'-Diethyl-6,7,6',7'-tetramethylthiacarbocyanin iodide	0.18	0.22	I–0.30	1.0	65
3,3'-Diethyl-6,7,6',7',9-pentamethylthiacarbocyanin iodide	0.18	0.22	II–0.32	1.0	53
3,3',9-Triethyl-6,7,6',7'-tetramethylthiacarbocyanin iodide	0.18	0.22	III–0.26	1.0	45
3,6,7,3',6',7'-Hexamethyl-9-ethylthiacarbocyanin	0.13	0.20	III–0.26	1.0	44

NOTES. I. Ethyl orthoformate. II. Ethyl orthoacetate. III. Ethyl orthopropionate.

* 0.15 gram of acetic anhydride added.

** 0.19 gram of propionic anhydride added.

Found %: N 13.60. $C_{16}H_{14}O_7N_4S$. Calculated %: N 13.79.

Dyes

3,3'-Diethyl-4,5,4',5'-tetramethylthiacarbocyanin iodide. A mixture of 0.16 g of ethylethyl sulfate of 2,4,5-trimethylbenzothiazole, 0.15 g of ethyl orthoformate, and 0.5 ml of pyridine was heated for an hour on an oil bath at 130-135°. Ether was added to the solution, the tarry precipitate being dissolved in ethyl alcohol, and the dye being recovered by adding an equal volume of a 10% solution of potassium iodide. The yield was 0.10 g (71% of the theoretical). M.p. 240-241°. Dull grayish-blue needles with a m.p. of 243-245° after crystallization from ethyl alcohol.

Found %: N 5.23. $C_{25}H_{29}N_2S_2I$. Calculated %: N 5.11.

3,3'-Diethyl-4,5,4',5',9'-pentamethylthiacarbocyanin iodide. This was synthesized, like the preceding dye, from ethyl orthoformate (0.16 g). The yield was 57% of the theoretical. Dark-green needles (from ethyl alcohol), m.p. 222-223°.

Found %: N 4.86. $C_{26}H_{31}N_2S_2I$. Calculated %: N 4.98.

3,3',9-Triethyl-4,5,4',5'-tetramethylthiacarbocyanin iodide. This was synthesized, like the dye without a chain substituent, by condensing 0.35 g of 2,4,5-trimethylbenzothiazole ethylethyl sulfate with 0.26 g of ethyl

TABLE 2 (continued)

Appearance	M.p.(with decom-position)	Absorption maximum (in mμ)	% N found	Calculated	
				Formula	% N
Lustrous dark-green needles	248°	568	5.08	$C_{25}H_{29}N_2S_2I$	5.11
Thin dark-violet needles	234	552	5.16	$C_{26}H_{31}N_2S_2I$	4.98
Minute dark-green prisms	229	556	4.86	$C_{27}H_{33}N_2S_2I$	4.86
Brownish-red prisms	206	551	5.16	$C_{25}H_{29}N_2S_2I$	5.11
Dark-green needles with a golden sheen	262	566	5.26	$C_{25}H_{29}N_2S_2I$	5.11
Blue-violet prisms	223	550	5.17	$C_{26}H_{31}N_2S_2I$	4.98
Brown prisms with a green tinge	208	554	5.01	$C_{27}H_{33}N_2S_2I$	4.86
Dark-green prisms with a golden sheen	260	570	4.97	$C_{25}H_{29}N_2S_2I$	5.11
Red-violet needles	275	554	4.84	$C_{26}H_{31}N_2S_2I$	4.98
Dark-blue needles	248-249	558	4.66	$C_{27}H_{33}N_2S_2I$	4.86
Red-violet prisms	253	554	4.96	$C_{25}H_{29}N_2S_2I$	5.11
Red-brown prisms with a greenish sheen	275	568	5.19	$C_{25}H_{29}N_2S_2I$	5.11
Grayish-blue needles	271	553	5.03	$C_{26}H_{31}N_2S_2I$	4.98
Green prisms	255	557	4.84	$C_{27}H_{33}N_2S_2I$	4.86
Brownish-red prisms	257	554	5.07	$C_{25}H_{29}N_2S_2I$	5.11
Green prisms with a golden sheen	287-288	568	5.06	$C_{25}H_{29}N_2S_2I$	5.11
Grayish-blue prisms	272-273	553	5.12	$C_{26}H_{31}N_2S_2I$	4.98
Dark-green prisms with a golden sheen	242-243	557	4.70	$C_{27}H_{33}N_2S_2I$	4.86
Minute dark-red prisms	253-254	555	5.26	$C_{25}H_{29}N_2S_2I$	5.11

orthoformate in 2 ml of pyridine. After the dye had been precipitated with ether, it was converted into the iodide in alcohol solution. The yield was 41.4% of the theoretical. Dark-green prisms with a golden sheen (from ethyl alcohol). M.p. 218-220°.

Found %: N 5.01. $C_{27}H_{33}N_2S_2I$. Calculated %: N 4.86.

3,4,5,3',4',5'-Hexamethyl-9-ethylthiacarbocyanin iodide. This was synthesized by heating 0.3 g of 2,4,5-trimethylbenzothiazole methylmethyl sulfate with 0.26 g of ethyl orthoformate, 1 ml of pyridine, and 0.05 g of acetic anhydride to 130° for 1 hour. The dye was precipitated with ether and converted into the iodide in the usual manner. The yield was 44.4% of the theoretical. The preparation was purified by double recrystallization from ethyl alcohol. Red-brown prisms with a m.p. of 210-211°. Absorption maximum at 550 mμ .

Found %: N 5.03. $C_{25}H_{27}N_2S_2I$. Calculated %: N 5.11.

4,6,4',6'-, 4,7,4',7'-, 5,6,5',6'-, 5,7,5',7'- and 6,7,6',7'-Tetramethylthiacarbocyanins. The 3,3'-diethyltetramethylthiacarbocyanins were synthesized by refluxing the respective trimethylbenzothiazoles with a 10% excess of ethyl p-toluenesulfonate for 6 hours on an oil bath at 140-150°. The quaternary salts of the 3,3'-diethyl derivatives were synthesized at 130-135°. Anhydrous pyridine and the ortho ester of the carboxylic acid were added to the quaternary salt (sometimes acetic or propionic anhydride was used), and the mixture was heated to 130-135° for 1 hour. The cooled reaction solution was diluted with ether, the precipitate or tarry mass thrown down being dissolved by boiling in ethyl alcohol, and the dye being recovered by adding an equal volume of a 10% solution of potassium iodide.

The dye was purified by crystallizing it from ethyl alcohol until its melting point remained constant; it was dried at 50-60° in vacuo over phosphoric anhydride before being analyzed. The dyes' synthesis conditions, properties, and analysis results are given in Table 2.

The absorption curves of the dyes were plotted in a $1 \cdot 10^{-4}$ molar solution in ethyl alcohol, using a Koenig-Martens spectrophotometer.

SUMMARY

1. Twenty-three symmetrical tetramethylthiacarbocyanins have been synthesized, containing methyl groups at various positions in the benzene rings of the heterocyclic residues. 2,4,5-, 2,4,7, and 2,5,7-trimethylbenzothiazoles have been synthesized, plus some derivatives of these bases.

2. It has been shown that the transition from dimethyl- to tetramethylthiacarbocyanins always involves a shift of the dye's absorption maximum toward the longer wave-lengths of the spectrum, the entrance of the methyl groups at the 5,5' and 6,6' positions producing a greater bathochromic shift.

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Received August 10, 1950

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THE EFFECT OF ACTIVATED CHARCOAL UPON THE OXIDATION OF PAPAVERINE BY ATMOSPHERIC OXYGEN

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One of the tests of the quality of pharmacopeial papaverine hydrochloride is its reaction with concentrated sulfuric acid. *The Pharmacopeia of the USSR* (8th ed.), like the pharmacopeias of several other countries, requires that papaverine hydrochloride dissolve in concentrated sulfuric acid without producing any coloration. A product that is not pure enough usually turns the solution violet.

In his time, Merck [1], who discovered papaverine, thought that the appearance of this coloration was a characteristic property of papaverine. Hesse [2] subsequently recrystallized papaverine acid oxalate and secured a product that did not cause any coloration when tested with concentrated sulfuric acid. Hesse thus showed that the appearance of a coloration when papaverine was dissolved in sulfuric acid had to be attributed to some unknown impurity in the papaverine. The same author [3] worked on the problem of isolating this impurity from commercial papaverine; he reported that he had isolated a new substance, which he called papaveramine. This substance produced a strong violet coloration when dissolved in concentrated sulfuric acid. Somewhat later Pictet and Kramer [4] also worked on the problem of isolating from commercial papaverine the impurity whose presence in the papaverine produces the violet coloration during the test with concentrated sulfuric acid. These researchers found no papaveramine, though they did isolate a substance that produced a violet coloration when dissolved in sulfuric acid. This substance proved to be the alkaloid cryptopine.

Ever since, it has been established doctrine in scientific circles that the violet coloration that appears when papaverine is tested with sulfuric acid is due to the presence of cryptopine. However, as our own researches have indicated, the problem of the appearance of the violet coloration when papaverine is dissolved in sulfuric acid must be explained otherwise. The present research was undertaken to shed light upon this cause.

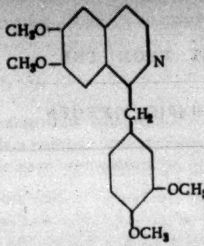
In the course of a long study of the problem of refining the papaverine secured from opium into a pharmacological product we discovered one interesting fact. We noticed that even absolute papaverine, which causes no coloration when dissolved in sulfuric acid, can be converted under certain conditions into a product that does produce this coloration. Upon a more detailed investigation of this phenomenon we found that this transformation of papaverine takes place in the following instances. First, this transformation occurs most readily when activated charcoal is used to refine aqueous solutions of papaverine. Second, a similar change in the papaverine, though not so pronounced occurs when the base papaverine is recovered from hot aqueous solutions of its salts by ammonia or other alkalies.

These indicate beyond the shadow of a doubt that the reason for the appearance of a violet color when papaverine is tested with sulfuric acid is the presence of some product of a transformation of the papaverine itself.

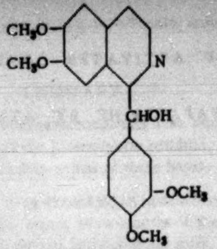
It is most likely that this product is a product of the oxidation of papaverine.

We know from the literature that the substance that is an oxidation product of papaverine and is also able to bring about a violet coloration when dissolved in concentrated sulfuric acid is papaverinol.

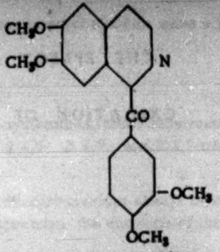
Stuchlik [5] synthesized papaverinol by reducing papaveraldine—a product first obtained by Goldschmidt [6] by oxidizing papaverine. Papaverinol is thus a product of the intermediate oxidation of papaverine to papaveraldine, as may be seen from their structural formulas:



Papaverine



Papaverinol



Papaveraldine

Inasmuch as the structural formula for papaverine contains a readily oxidizable methylene group located between two rings, it is highly probable that during the refining of papaverine the latter may be partially oxidized to papaverinol. The presence of the latter as an impurity in the papaverine would bring about the violet coloration when the papaverine is tested with sulfuric acid. It would be desirable, however, to produce experimental proof that this is so.

As we stated above, the most striking change in papaverine (in so far as its behavior in the sulfuric acid test is concerned) takes place when aqueous solutions of its salts are treated with activated charcoal. We therefore resolved to make use of this phenomenon in setting up our experiment.

We did this by adding enough activated charcoal to a solution of pure papaverine hydrochloride to have nearly all the alkaloids absorbed by the charcoal after air had been blown through the heated solution. Then the alkaloids were desorbed by chloroform. Two oxidation products of papaverine, papaveraldine and papaverinol, were found in the resulting chloroform solution.

This experiment proved that papaverine could be oxidized by atmospheric oxygen in the presence of activated charcoal yielding papaverinol, a substance that produces a violet coloration when it is dissolved in sulfuric acid.

We think the following fact should also be cited by way of supplementary proof: papaverine produced synthetically, in which no cryptopine or any other opium alkaloid can be present, almost always produces a violet coloration when tested with sulfuric acid (unless it is specially purified).

With papaverinol at our disposal, we were greatly interested in determining the sensitivity of the reaction of this substance with sulfuric acid that produces a violet coloration. We found that this is an extremely sensitive reaction, viz.: the coloration is still perceptible at a dilution of 1:1,000,000, whereas the color is nearly imperceptible in a layer 16 mm thick (diameter of the test tube) at a dilution of 1:2,000,000. The test temperature was +23°.

Once we know the sensitivity of this reaction, we can calculate that a 0.025% trace of papaverinol in the papaverine suffices to produce a violet coloration when papaverine is tested with sulfuric acid as prescribed by the pharmacopeia.

EXPERIMENTAL

6 grams of pure papaverine hydrochloride was dissolved in 250 ml of water, and 20 g of activated charcoal (O.U.brand) was added to the solution. A current of air was then passed through the solution at 70° for 15 hours. The charcoal was filtered out, and a dark amorphous precipitate weighing 0.3 g was thrown down from the solution by adding ammonia until the reaction was alkaline. The bulk of the alkaloid was obviously adsorbed by the activated charcoal.

The activated charcoal was triply extracted with chloroform, using 150 ml in each extraction. After the chloroform had been driven off, the residue consisted of a dark crystalline mass weighing 3.6 g. The residue was dissolved in 100 ml of 10% sulfuric acid. The small amount of undissolved residue was filtered out. Then the solution was diluted with twice its volume of water and agitated three times with chloroform, using 80 ml of the latter each time. The acid solution was then alkalinized with ammonia until the odor of the latter was clearly perceptible, and the alkaline solution was again agitated with chloroform 3 times, using 80 ml each time. The chloroform extracts, secured from the acid as well as from the alkaline solutions, were dried separately with calcined sodium sulfate. Driving off the chloroform from the extract obtained by extracting the acid aqueous solution yielded 2 g of a crystalline residue. Driving off the solvent from the extract obtained by extracting the alkaline solution yielded 1.3 g of a dark amorphous mass.

The first residue was dissolved by heating it in 50 ml of a 5% hydrochloric acid solution. The solution was filtered while hot. As it cooled, crystals settled out as minute elongated yellow needles. The 2.2 g of yellow crystals was recrystallized from 50 ml of 5% hydrochloric acid. The new crystalline precipitate was dissolved by heating it in 15 ml of ethyl alcohol. When aqueous ammonia was added to this alcoholic solution, a fine, white, crystalline precipitate was rapidly thrown down. The precipitate weighed 1.2 g, m.p. 209-210°. Its mixed melting point with the papaveraldine we had synthesized from papaverine by the Pschorr method [7], as modified by Kabachnik and Zitser [8], exhibited no depression.

The second, amorphous precipitate was dissolved by heating it in a small quantity of methanol. After the solution had cooled and stood for some time, 0.6 g of a dark, crystalline precipitate settled out. The precipitate was dissolved in 20 ml of weak hydrochloric acid. The acid solution was clarified with activated charcoal, and ammonia was added to the clarified and filtered solution until its odor became perceptible. A brown tar was thrown down, which solidified rapidly. The solid tar was dissolved by heating it in 10 ml of 60% methanol, and the solution was hot-filtered. After the solution had cooled and stood for some time, 0.4 g of a light crystalline precipitate settled out. The precipitate was again recrystallized from 10 ml of 60% methanol, yielding 0.3 g of white crystals with a m.p. of 136-137°. The mixed melting point with the papaverinol we had synthesized by the Stuchlik method [5] exhibited no depression.

SUMMARY

1. It has been proved that papaveraldine and papaverinol are produced when papaverine is oxidized by atmospheric oxygen in the presence of activated charcoal. In view of the well-known fact that papaverinol dissolves in concentrated sulfuric acid, forming a violet solution, this fact that we have established proves that the impurity in papaverine that produces a violet color when the latter is tested with sulfuric acid is papaverinol.

2. The sensitivity of the color reaction of papaverinol with sulfuric acid has been determined.

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Received October 7, 1950

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SOME NEW ALICYCLIC ISOMERS OF AROMATIC HYDROCARBONS

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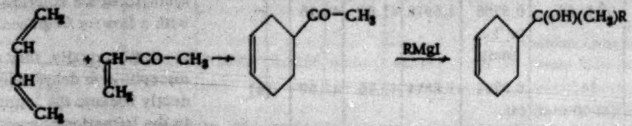
In one of the previous reports from our laboratory, we have described the results of our experiments on the synthesis of hydroaromatic alcohols — the isomers, homologs, and analogs of α-terpineol — from the condensation products of diene hydrocarbons with methyl vinyl ketone as follows (for divinyl) [1]:

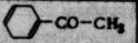
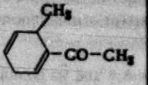
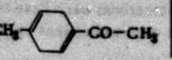


We were interested in extending these researches to the synthesis, by the same method of more highly unsaturated alcohols and in employing the latter to synthesize triene alicyclic hydrocarbons, isomers of the alkyl benzenes.

The initial substances we used in these syntheses were the condensation products of 1,3-dienes: divinyl, isoprene, and piperylene, with methyl ethynyl ketone.

The condensation product of divinyl and methyl ethynyl ketone has been described by one of the present authors [2]. The other two diene ketones have been synthesized for the first time. The constants of the diene ketones and the properties of some of their derivatives are given in Table 1.

TABLE 1

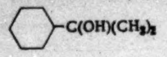
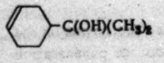
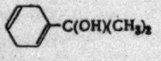
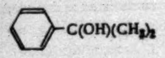
Substance	B.p. at 20 mm	d_4^{20}	n_D^{20}	Experimental	Calculated	Melting point	
						Semicarbazone	Nitrophenylhydrazone
	93.5-94.5*	1.0168	1.5150	36.12	36.02	199.5-200.5	203-204
	95.5-96	0.9726	1.4985	41.08	40.64	171-172	185-186
	111-111.5	0.9872	1.5062	41.00	40.64	208-209	196-198

When isoprene and piperylene are condensed with methyl ethynyl ketone, we may expect two products in each condensation. Numerous experiments on the condensation of these hydrocarbons with unsaturated aldehydes, ketones, nitriles, and acids indicate that in the former case the products always have the radicals at the para position, while in the latter they are always at the ortho position [3].

The condensation of isoprene and piperylene with methyl ethynyl ketone likewise resulted in para and ortho products, respectively. This was proved by synthesizing p-cymene from the condensation product of isoprene and methyl ethynyl ketone, and of o-cymene from the condensation product of piperylene with the same ketone, as the result of the transformations described below.

The action of CH_3MgI upon the 1,4-cyclohexadiene ketones listed in Table 1 under the customary conditions yielded cyclohexadiene alcohols that are not described in the literature: dimethyl-(cyclohexadienyl)-carbinol and its homologs. Of these alcohols only dimethyl-(cyclohexadien-1,4-yl)-carbinol was isolated in the pure state. The constants of this alcohol are compared with those of its more highly saturated and unsaturated analogs in Table 2.

TABLE 2

Substance	B.p. at 20 mm	d_4	n_D	MR_D		References
				Experimental	Calculated	
	96°	0.9280 (at 18°)	1.472	42.92	43.09	[4]
	95.5-96	0.9479 (at 20°)	1.4824	42.20	42.62	[1]
	97.5-98	0.9788 (at 20 mm)	1.5012	41.61	42.15	–
	94 (at 13 mm)	0.9724 (at 18.5°)	1.5314	43.36	41.69	[4]

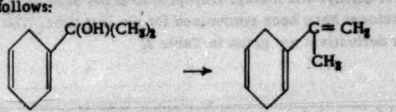
We see in Table 2 that the boiling point, the specific gravity, and the refractive index of the diene alcohol are somewhat higher than those of its more highly saturated analogs, as might have been expected. Its specific gravity is higher, though its refractive index is considerably lower, than that of dimethylphenylcarbinol.

The tertiary alcohols of the cyclohexadiene series we have synthesized are colorless liquids with a flowery fragrance.

Chemically, they are highly susceptible to dehydration, evidently because the latter results in the formation of a conjugated system of bonds.

The alcohols are dehydrated even when distilled in vacuo. This occurs so readily in the dimethyl-(methylcyclohexadienyl)-carbinols that we were unable to isolate these alcohols in the pure state. The alcohols are dehydrated very readily when distilled with a 5% solution of oxalic acid or in vacuo with an iodine crystal.

The dehydration of the cyclohexadiene alcohols ought to result in the formation of triene hydrocarbons, isomers of the aromatics, as follows:



These hydrocarbons are actually formed when dehydration is carried out by the first or second method. When iodine is employed for dehydration, the reaction products are the corresponding aromatic hydrocarbons.

No alicyclic hydrocarbons with a 1,4-cyclohexadiene ring and a vinyl group in the side ring have yet been described in the literature, it being a moot point whether they could exist or not. The references in the literature led us to think that hydrocarbons of this sort ought to be readily isomerized, possibly at the instant of their formation, into derivatives of benzene.

Of the C_nH_{2n-6} alicyclic hydrocarbons, only 1,1-dimethyl-4-methylenecyclohexadiene-2,5 and its homologs have been described in the literature at length thus far [4]. In spite of the fact that these hydrocarbons each have two radicals attached to the same ring carbon atom, they are readily isomerized by hydrochloric acid to benzene derivatives, one of the radicals shifting to the ortho position.

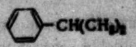
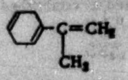
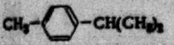
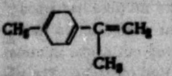
We have synthesized two vinylcyclohexadiene hydrocarbons in a fairly pure state: isopropenylcyclohexadiene-1,4 and 4-methylisopropenylcyclohexadiene-1,4. When dimethyl-(2-methylcyclohexadien-1,4-yl)-carbinol was dehydrated, the alicyclic hydrocarbon was partially dehydrated to its aromatic isomer: o-cymene. The two synthesized alicyclic hydrocarbons were colorless liquids with a rather sharp aromatic odor that differed from the odor of the corresponding aromatic hydrocarbons. Their constants are listed in Table 3.

Table 3 indicates that the vinylcyclohexadiene hydrocarbons have much higher boiling points, specific gravities, and refractive indexes than their aromatic isomers.

There is no doubt about the formulas assigned to these hydrocarbons, since the initial alcohols can be dehydrated in only one way. These formulas are borne out by all the chemical properties of the substances in question.

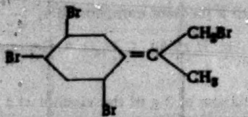
We investigated the isomerization, bromination, and oxidation of the synthesized hydrocarbons, as well as their condensation with maleic anhydride. Our experiments indicated that the vinylcyclohexadiene hydrocarbons

TABLE 3

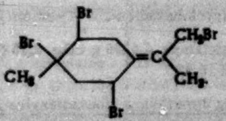
Substance	B.p.	d_4^{20}	n_D^{20}	MR_D		References
				Experimental	Calculated	
	152-153	0.8640	1.4947	40.54	40.16	[4]
	172-176	0.9068	1.5216	40.40	40.16	–
	177	0.8570	1.4908	45.34	44.78	[4]
	192-196	0.8903	1.5156	45.50	44.78	–

are readily isomerized to aromatic hydrocarbons by hydrogen chloride. Cumene was produced from isopropenylcyclohexadiene in this manner, as were o- and p-cymenes from o- and p-methylisopropenylcyclohexadienes, respectively. The position of the radicals in the latter substances was established by oxidation, the o-cymene yielding dimethylphthalide and the p-cymene p-[hydroxyisopropyl]-benzoic acid.

When the vinylcyclohexadiene hydrocarbons were brominated in chloroform, they readily added no more than two molecules of bromine, yielding tetrabromides. We isolated the crystalline tetrabromides of two of the hydrocarbons in the pure state. The liquid isomers are apparently produced together with the crystalline tetrabromides. The structure of the tetrabromides was not established, but it is highly probable that their formulas are as follows, on the basis of the assumption that one of the bromine molecules is added at one end of the conjugated system:



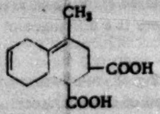
and



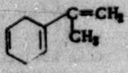
The quantity of potassium permanganate consumed when isopropenylcyclohexadiene was oxidized with an excess of a 5% permanganate solution was the equivalent of 5 gram atoms of oxygen. Acetophenone, identified as its 2,4-dinitrophenylhydrazone, was identified among the oxidation products, though no acetone was found. We were unable to isolate organic acids.

This established that oxidation of the hydrocarbon did not involve the rupture of the ring, but merely its dehydrogenation, the isopropenyl group being normally oxidized to an aceto group.

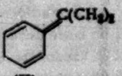
Heating the isopropenylcyclohexadiene with an equimolecular quantity of maleic anhydride yielded a crystalline condensation product, from which we secured a crystalline dibasic acid. The structure of this acid was fixed by the method of synthesis employed. It can be assigned the following formula:



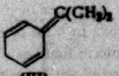
Analysis of the experimental data for isopropenylcyclohexadiene indicates that 5 out of the 6 possible formulas for the C_9H_{12} alicyclic hydrocarbon must be eliminated:



(I)

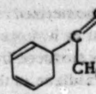


(II)

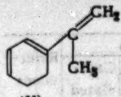


(III)

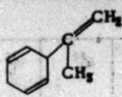
Two of them, (II) and (III), require that acetone be formed during oxidation, which is not the case. The substance with the formula (VI) does not possess conjugated double bonds and hence cannot be condensed with maleic anhydride. Thus this latter formula is likewise excluded. The substance with the formula (V) ought to exhibit a high exaltation of the molar refraction, inasmuch as it possesses a system of three conjugated double bonds. The hydrocarbon we synthesized possesses low exaltation, so that Formula (V) is not very likely. Formula (IV) must also



(IV)



(V)



(VI)

be discarded, as it is difficult to imagine that such a hydrocarbon can be formed when dimethylcyclohexadienylcarbinol is dehydrated. This isomerization would have to involve the loss of conjugation of the double bonds in the ring and the side chain. Hence, the structure of isopropenylcyclohexadiene-1,4 may be regarded as established.

EXPERIMENTAL

Synthesis of dimethyl-(cyclohexadien-1,4-yl)-carbinol. The initial ketone required for the synthesis was prepared by condensing divinyl with methyl ethynyl ketone at 110° in a toluene solution [3].

10 g of the ketone was added, with chilling and stirring, to a solution of an organomagnesium compound prepared from 3 g of magnesium and 15 g of methyl iodide in 100 ml of absolute ether. After the mixture had stood for 4 hours and been heated for 1 hour (an abundant crystalline precipitate settling out), it was poured into a flask containing a solution of ammonium chloride and pieces of ice. After the salts had been filtered out of the solution, the latter was dried with calcined Na_2SO_4, the ether was driven off, and the alcohol was distilled in vacuo. The substance decomposed violently toward the end of distillation, so that the first distillation must be run at as low a pressure as possible. We distilled the alcohol at 10 mm. It boils at 85-86° at this pressure. The constants of the alcohol are given in Table 1. The yield was 65%, based on the ketone.

Dimethyl-[cyclohexadien-1,4-yl]-carbinol is a colorless liquid with a pleasant camphor odor.

0.1719 g substance: 0.4950 g CO_2; 0.1582 g H_2O. Found %: C 78.58; H 10.30. $C_9H_{14}O$. Calculated %: C 78.21; H 10.21.

Dehydrating dimethylcyclohexadienylcarbinol. a) The slow distillation of 3 g of the alcohol at a 100-mm vacuum yielded 2.1 g of a hydrocarbon with a b.p. of 172-174° and n_D^{20} 1.5200. The hydrocarbon readily decolorized bromine water and a solution of potassium permanganate.

b) Distilling 2.6 g of the alcohol in vacuo with a small iodine crystal yielded 2.2 g of a distillate with a b.p. of 151-153° and d_4^{20} 0.8640 and n_D^{20} 1.4928, which did not decolorize bromine water or a permanganate solution. Its constants were those of cumene.

c) 2.6 g of the alcohol was distilled with a 5% solution of oxalic acid. The hydrocarbon recovered from the water [2.1 g (98%)] had the constants cited in Table 2, and its chemical properties did not differ from those of the hydrocarbon produced by the method (a).

0.1210 g substance: 0.3996 g CO_2; 0.1073 g H_2O. Found %: C 90.12; H 9.92. C_9H_{12}. Calc.%: C 89.94; H 10.06.

It should be noted that the unsaturated hydrocarbon synthesized always contained cumene as an impurity, which was readily eliminated by distillation, since there is a difference of some 20° between the boiling point of cumene and that of unsaturated hydrocarbon.

Isomerization of isopropenylcyclohexadiene. 2 g of the unsaturated hydrocarbon was heated on a water bath for 1 hour together with 2.5 ml of acetic acid and 1 ml of conc. hydrochloric acid. Then the mixture was diluted with water, and the hydrocarbon was distilled with steam. After having been washed with a NaOH solution and dried with $CaCl_2$, the hydrocarbon was distilled at ordinary pressure. B.p. 152-153°; d_4^{20} 0.8640; n_D^{20} 1.4946. The figures given in the literature for cumene have been cited earlier.

Bromination of isopropenylcyclohexadiene. A solution of bromine in chloroform was added to a solution of 0.36 g of the hydrocarbon in 5 ml of ether until no more decolorization occurred. The bromine consumed totaled 1.1 g. After the chloroform had been driven off in vacuo, the crystalline residue was transferred to a filter and washed by suction-filtering with alcohol. The 0.87 g yield of crystals with a m.p. of 110-114° thus purified constituted 60% of the theoretical. The substance was sparingly soluble in alcohol, and freely soluble in chloroform and ether. It was recrystallized by precipitating it with alcohol from a chloroform solution. The melting point of the substance thus purified was 113-114°. Colorless lamellae.

0.1182 g substance: 0.2005 g AgBr. Found %: Br 72.18. $C_9H_{12}Br_4$. Calculated %: Br 72.67.

Oxidizing isopropenylcyclohexadiene. 2.4 g of the hydrocarbon was agitated for 6 hours with a 5% solution of potassium permanganate containing magnesium sulfate. The excess permanganate was removed by adding manganese sulfate. Oxidation consumed 10.2 g of permanganate. Then the solution was distilled with steam. The upper layer of the distillate was separated, dried with $CaCl_2$, and distilled, yielding about 0.6 g of the unreacted hydrocarbon (n_D^{20} 1.5210) and a residue that proved to be acetophenone. When the residue was treated with an acetic acid solution of 2,4-dinitrophenylhydrazine, the characteristic orange dinitrophenylhydrazone settled out; it had a m.p. of 235-237°, and its mixed melting point with a known preparation of acetophenone dinitrophenylhydrazone exhibited no depression.

The crystalline precipitate of the dinitrophenylhydrazone obtained from the aqueous part of the distillate had a m.p. of 170-190° before recrystallization, whereas the acetone dinitrophenylhydrazone had a m.p. of 128°. The m.p. of the substance was 237° after recrystallization from a mixture of alcohol and ethyl acetate, the same as that of the dinitrophenylhydrazone obtained from the bulk of the substance.

The residue left in the flask was filtered out, distilled with steam, evaporated to a small volume, and acidulated with sulfuric acid. Carbon dioxide was evolved. Repeated treatment of the liquid with ether did not succeed in isolating from it any perceptible quantity of acid.

Condensing isopropenylcyclohexadiene with maleic anhydride. A solution of 0.48 g of the hydrocarbon and 0.5 g of maleic anhydride in 5 ml of toluene was heated on a boiling water bath for 5 hours, a crystalline condensation product settling out. Then the liquid was boiled with 10 ml of a 10% KOH solution, and the alkaline solution was acidulated with hydrochloric acid. An oil separated out, which crystallized when boiled with water. This yielded 0.4 g (43%) of a dibasic acid, which had a m.p. of 167-169° before recrystallization. The substance had a m.p. of 178° in a sealed capillary after it had been recrystallized from aqueous alcohol. Colorless leaflets, freely soluble in alcohol, ether, and chloroform,and sparingly so in water.

0.1928 g substance: 0.4684 g CO_2; 0.1190 g H_2O. 0.1082 g substance:. 9.15 ml 0.1 N NaOH. Found %: C 66.30; H 6.91; equivalent 118.3. $C_{13}H_{16}O_4$. Calculated %: C 66.08; H 6.83; equivalent 118.1.

Synthesis of 4-methylacetylcyclohexadiene-1,4. 14.5 g of methylacetylcyclohexadiene was synthesized from 13 g of ethoxyvinylacetylene and 15 ml of isoprene (an excess) by the method previously described. The yield was 82%. The constants of the substance are given in Table 1.

0.1066 g substance: 0.3113 g CO_2; 0.0844 g H_2O. Found %: C 79.69; H 8.86. $C_9H_{12}O$. Calculated %: C 79.37; H 8.88.

The semicarbazone and the p-nitrophenylhydrazone of the ketone were prepared in the usual manner. The semicarbazone consisted of colorless leaflets, freely soluble in alcohol and sparingly in water. It was recrystallized from dilute alcohol. The p-nitrophenylhydrazone consisted of orange prisms, freely soluble in ethyl acetate, and sparingly in alcohol. It was recrystallized from a mixture of ethyl acetate and alcohol.

When isoprene was heated with methyl ethynyl ketone in toluene to 150-180°, we obtained a substance whose constants differed sharply from those of the substance described above (b.p. 109.5-110.5°; d_4^{20} 0.9889; n_D^{20} 1.52).

Synthesis of 4-methylisopropenylcyclohexadiene-1,4. Dimethyl-(4-methylcyclohexadien-1,4-yl)-carbinol was prepared from 12.2 g of the ketone described above, 2.8 g of Mg, and 17 g of methyl iodide in the usual manner. When the substance was distilled in vacuo (20 mm), all the water was split out, yielding 10.5 g of a hydrocarbon (87% yield). The constants of the substance are given in Table 2.

0.1166 g substance: 0.3832 g CO_2; 0.1135 g H_2O. Found %: C 89.68; H 10.89. $C_{10}H_{14}$. Calculated %: C 89.48; H 10.52.

Brominating methylisopropenylcyclohexadiene. A solution of 0.49 g of the hydrocarbon in 10 ml of chloroform was chilled with a freezing mixture (ice + salt), and a chloroform solution of bromine was added until no more decolorization occurred. Two molecules of bromine were used up per molecule of the hydrocarbon.

After the chloroform had been driven off in vacuo, there was left in the flask a crystalline substance that had a m.p. of 123-124° after having been washed with alcohol. The yield of washed crystals totaled 0.6 g (35%, based on the tetrabromide).

The m.p. of the substance was 126° after recrystallization by means of reprecipitation from a chloroform solution by alcohol.

0.1116 g substance: 0.1834 g AgBr. Found %: Br 69.93. $C_{10}H_{14}Br$. Calculated %: Br 70.43.

The tetrabromide was freely soluble in chloroform and ether and sparingly so in ethyl alcohol.

Isomerization of methylisopropenylcyclohexadiene. A solution of 5 g of the hydrocarbon in a mixture of 15 ml of acetic and 5 ml of conc.hydrochloric acids was refluxed on a water bath for 1 hour, after which the mixture was distilled with steam. The upper layer of the distillate was separated, washed with a soda solution, and distilled, yielding 4.2 g of p-cymene. 84% yield. B.p. 174-176°; d_4^{20} 0.8583; n_D^{20} 1.4948.

0.1326 g substance: 0.4339 g CO_2, 0.1309 g H_2O. Found %: C 89.30; H 11.05. $C_{10}H_{14}$. Calculated %: C 89.48; H 10.52.

The substance did not decolorize bromine water.

Oxidizing the substance (2.7 g) with an excess of an alkaline solution of permanganate on water bath yielded p-isopropylbenzoic acid with a m.p. of 155-157° (1.0 g), plus a small amount (0.15 g) of terephthalic acid (identified as its dimethyl ester with a m.p. of 141°). Both of these substances are characteristic products of the oxidation of p-cymene.

Synthesis of 2-methylacetylcyclohexadiene-1,4. 12.8 g of the ketone was produced from 13 g of methoxyvinylacetylene and 25 ml of piperylene (a mixture of the cis and trans forms) by the usual method. 72% yield. The constants of this substance are given in Table 1.

0.1566 g substance: 0.4536 g CO_2; 0.1192 g H_2O. Found %: C 79.04; H 8.52. $C_9H_{12}O$. Calculated %: C 79.37; H 8.88.

The semicarbazone of the ketone consisted of colorless leaflets. It was precipitated slowly. It is distinguished by its sparing solubility. It was recrystallized from dilute alcohol. The p-nitrophenylhydrazone consisted of orange crystals. It was sparingly soluble in organic solvents. It was recrystallized from a mixture of ethyl acetate and alcohol.

Synthesis of dimethyl-(2-methylcyclohexadienyl-1,4)-carbinol and its dehydration. The carbinol was synthesized from 11.4 g of the ketone, 2.6 g of magnesium, and 16 g of methyl iodide in ether. Dehydration occurred even while the ether was being driven off. Distilling the substance in vacuo (20 mm) yielded a hydrocarbon whose constants approached those of o-cymene. B.p. 72-72.5° at 20 mm, 174-178° at 755 mm; d_4^{26} 0.8828; n_D^{16} 1.5056.

0.1191 g substance: 0.3917 g CO_2, 0.1132 g H_2O. Found %: C 89.75; H 10.63. $C_{10}H_{14}$. Calculated %: C 89.48; H 10.52.

The following constants are given in the literature for o-cymene: b.p. 175°; d_4^{16} 0,876; n_D^{24} 1.5006. The slight rise in the values of the specific gravity and the refractive index over the figures given in the literature is attributable to the presence of the alicyclic isomer as an impurity.

This is also indicated by the fact that the substance decolorizes bromine water. When the substance was brominated in chloroform, about one-quarter of the bromine calculated on the basis of the hexabromide was used. We were unable to isolate a crystalline polybromide.

When 5 g of the substance was heated with hydrochloric acid in acetic acid solution, we obtained 4 g of a substance (80% yield), which did not decolorize bromine water.

The substance's constants did not differ from those cited in the literature for o-cymene.

When 2 g of the substance was oxidized by heating it on a water bath with an excess of an alkaline solution of potassium permanganate and processed in the usual manner, we secured 0.5 g of dimethylphthalide, with a m.p. of 66-68°. This substance is a characteristic product of the oxidation of o-cymene.

SUMMARY

1. Acetylcyclohexadiene-1,4 and its 2- and 4-methyl substitution derivatives have been synthesized by condensing 1,3-diene hydrocarbons: divinyl, isoprene, and piperylene with methyl ethynyl ketone. The last two substances have been described for the first time.

2. The respective hydroaromatic tertiary alcohols – diethyl-(cyclohexadien-1,4-yl)-carbinol and its homologs – have been synthesized for the first time by reacting these ketones with CH_3MgI.

3. The unexplored isomers of cumene and the cymenes – isopropenylcyclohexadiene-1,4 and 4-methylisopropenylcyclohexadiene-1,4, plus the unpurified 2-methylisopropenylcyclohexadiene-1,4 – have been synthesized by dehydrating the alcohols.

4. It has been shown that HCl readily isomerizes all these hydrocarbons to aromatic hydrocarbons – cumene and the isomeric cymenes. Brominating them yields crystalline tetrabromides.

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Received December 17, 1950. Leningrad Institute of Aviation Instrument Construction

RESEARCH ON UNSATURATED CYCLIC HYDROCARBONS AND THEIR HALOGEN DERIVATIVES

XII. THE MECHANISM OF THE REACTIONS OF CONJUGATED HALOGENATION AND DEHALOGENATION

N.A.Domnin and V.A.Cherkasova

In our previous report [1] we showed that the conversion of 1,2-dibromocyclohexane into benzene by heating it with quinoline actually takes place via the formation of a six-membered ring with conjugated double bonds, as required by the first stage of the diagram suggested by one of the present authors [2] for the transformation of polyhalogenated derivatives of cyclohexane into aromatic compounds by heating them with quinoline.

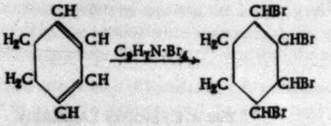
To prove the second stage of the schema (the formation of quinoline perbromates) we reacted cyclohexadiene-1,3 with three different quinoline perbromates (in the presence of quinoline), which we assumed might be formed in conjugated halogenation and dehalogenation: quinoline dibromide – $C_9H_7N{\cdot}Br_2$; quinoline hydrobromide dibromide, $C_9H_7N{\cdot}HBr{\cdot}Br_2$, and quinoline tetrabromide, $C_9H_7N{\cdot}Br_4$.

The experiments were run in a flask fitted with a dropping funnel and a reflux condenser, the mixture of cyclohexadiene-1,3 and one of the quinoline perbromates being heated in quinoline on an oil bath at 110-140° for several hours. The ultraviolet absorption spectrum of the reaction product was photographed to establish whether benzene had been formed from the cyclohexadiene-1,3 [1]. We found that cyclohexadiene-1,3 is converted to benzene when reacted with quinoline hydrobromide dibromide and quinoline dibromide, whereas it is converted into benzene and bromobenzene when reacted with quinoline tetrabromide.

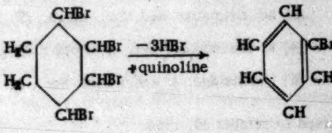
The production of bromobenzene may be readily explained as follows, in accordance with the schema suggested earlier.

1. Synthesis of cyclohexadiene-1,3.
2. Synthesis of quinoline tetrabromide.

3.



4.



All these facts confirm the second stage of the schema suggested [2] (the formation of quinoline perbromates).

EXPERIMENTAL

1. Reaction of cyclohexadiene-1,3 with quinoline tetrabromide in quinoline. 35 g of quinoline tetrabromide [3] was chilled, and 6 g of cyclohexadiene-1,3 was cautiously added (vigorous reaction), followed by 19.5 g of quinoline, and the mixture was refluxed for 1.5 hours at 130-140°. Then the fraction with a b.p. of 76-160° was driven off, washed with dilute sulfuric acid and with water, dried with calcium chloride, and distilled. This yielded two fractions: a) with a b.p. of 78-85° (1.85 g), and b) with a b.p. of 150-155° (2.35 g). Fraction 1 had a b.p. of 78-80.5° after distillation with metallic sodium, a n_D^{18} 1.4956, and contained halogen (Beilstein test). Spectroscopic analysis indicated that its absorption band differed from the absorption band of the cyclohexadiene-1,3 used for the reaction; it had the fine structure of benzene, obscured, however, by traces of bromobenzene and the unreacted cyclohexadiene-1,3. Distillation of Fraction 2 yielded 1.9 g of a transparent liquid with a b.p. of 152-158°; d_4^{18} 1.4620; n_D^{18} 1.5550; MR_D 34.46. $C_6H_5Br\ \Gamma_3$; Calculated MR_D 34.07. Spectroscopic analysis indicated that the

substance produced had a wholly different absorption from that of both cyclohexadiene-1,3 and benzene, and that approximately 90% of the product was bromobenzene.

2) Reaction of cyclohexadiene-1,3 with quinoline hydrobromide dibromide in quinoline. 43 g of $C_9H_7N{\cdot}HBr{\cdot}Br_2$ [4,5] was chilled, and 8 g of cyclohexadiene-1,3 was cautiously added (vigorous reaction), followed by 27 g of quinoline. The contents of the flask were refluxed for about 1 hour at 110-140°, and then a fraction with a b.p. of 70-110° was distilled off. Distillation of the washed and dried product with metallic sodium yielded a fraction with a b.p. of 80-83° (2.3 g), a colorless transparent liquid that crystallized in a freezing mixture (snow and salt), whose constants agreed with those of benzene: d_4^{17} 0.8828; $n_D^{17.3}$ 1.5035; MR_D 26.12; calculated 26.31; bromine number 0.9. Ultraviolet absorption spectroscopy indicated that the product contained 90-95% of benzene.

3) Reaction of cyclohexadiene-1,3 with quinoline dibromide in quinoline. 4.1 g of cyclohexadiene-1,3 and 16 g of quinoline were added to 22 g of $C_9H_7N{\cdot}Br_2$ (prepared by us as a crystalline mass by adding the calculated quantity of bromine to a thoroughly chilled emulsion of quinoline in water). After refluxing for 40 minutes at 110-130°, a fraction with a b.p. of 70-95° was distilled off. After it had been washed and dried (1.8 g), it had a b.p. of 76-80° and a n_D^{16} 1.4870 (n_D^{20} 1.5017 for benzene and n_D^{20} 1.4742 for cyclohexadiene-1,3). It was found spectroscopically that the product contained about 20% of benzene.

SUMMARY

1. Ultraviolet absorption spectroscopy has been used to prove that the low-boiling fraction (b.p. 78-80.5°) of the product obtained by reacting cyclohexadiene-1,3 with quinoline tetrabromide in quinoline contains benzene, bromobenzene, and cyclohexadiene-1,3, while the high-boiling fraction (b.p. 152-158°) contains about 90% of bromobenzene.

2. The reaction of cyclohexadiene-1,3 with quinoline hydrobromide dibromide in quinoline yields a mixture of products that contains 90-95% of benzene.

3. The reaction of cyclohexadiene-1,3 with quinoline dibromide in quinoline yields a mixture of products that contains about 20% of benzene.

4. It has been shown that the second stage of the transformation of polyhalogenated derivatives of cyclohexane into aromatic compounds by heating them with quinoline involves the formation of quinoline perbromates, as indicated in the second stage of the schema suggested.

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Received December 30, 1950.

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RESEARCH ON THE HYDROSULFATES OF THE ALKALI ELEMENTS

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The hydrosulfates of the alkali elements are produced when sulfuric acid acts upon their chlorides, normal sulfates, and other salts under certain conditions. The utilization of hydrosulfates for the acidic decomposition of certain ores and for the sulfating fusion of different substances in analytical chemistry and chemical technology is largely based upon their conversion at high temperature into pyrosulfates and then into normal sulfates, sulfur trioxide being given off. Far from enough work has been done on the physicochemical properties of the hydrosulfates. There is almost no information, for example, on their hydration, melting points, and limits of thermal stability.

We have prepared the pure hydrosulfates of all the alkali elements, determined the melting points of these compounds, investigated the behavior of the hydrosulfates when heated, and established the temperatures at which they begin to change into pyrosulfates.

The information on the production of lithium hydrosulfate is highly contradictory. Weber [1] and Kobbe [2] believe that lithium does not constitute a compound with the composition of $LiHSO_4$ at all. According to Schultz [3], this compound is precipitated from a solution of the normal sulfate in sulfuric acid, while Lescoeur [4] asserts that the salt is produced only when the sulfuric acid employed is a monohydrate. Dunnicliff's efforts [5] to crystallize the hydrosulfate from aqueous solutions of normal lithium sulfate that contained a large excess of sulfuric acid resulted in the formation of crystals of the monohydrate of normal lithium sulfate, more or less contaminated with sulfuric acid. The acid is eliminated entirely by the action of ether. The composition of the crystals was as follows: 38.71% sulfuric acid; 57.02% normal lithium sulfate; 4.27% water. According to Dunnicliff, the hydrosulfate ought to have 47.11% of sulfuric acid and 52.89% of the normal lithium sulfate.

The hydrosulfates of sodium and potassium were prepared by the generally used method of reacting the respective chlorides or normal sulfates with sulfuric acid.

Erdmann [6] obtained rubidium hydrosulfate as a bright, oily, slightly mobile liquid by dissolving rubidium salts with a volatile acid in sulfuric acid and evaporating in a platinum cup. When chilled, the hydrosulfate solidified into a beautiful ray-like mass. Dunnicliff [5] obtained rubidium hydrosulfate by treating the chloride or the normal sulfate with the theoretical quantity of sulfuric acid. The solution was evaporated to dryness, the residue being melted. The resulting product was pulverized in a hot agate mortar and then treated with seven times its weight of absolute alcohol and washed with ether. The percentage of sulfuric acid in the residue was found to be 29.93%. The theoretical percentage of H_2SO_4 in rubidium sulfate is stated by the author to be 26.86%. Endeavors to secure rubidium hydrosulfate by treating the nitrate with a slight excess of sulfuric acid and then evaporating the solution and heating the residue were unsuccessful, for it was extraordinarily difficult to eliminate the traces of acid even by prolonged heating. Browning [7] met with the same lack of success.

Kirchhoff and Bunsen [8] produced cesium hydrosulfate by treating the carbonate with an excess of sulfuric acid and then heating the mixture until the excess acid had been eliminated. The cooled crystalline mass was dissolved in water, the resulting hydrosulfate settling out as small crystals when the solution was slowly heated. Dunnicliff [5] secured cesium hydrosulfate by the same method he used to get the rubidium hydrosulfate.

As Berthelot [9] pointed out, sodium and potassium pyrosulfates are converted into the hydrosulfates when they are dissolved in water. We employed this method to secure pure hydrosulfates of all the alkali elements. Samples of the pyrosulfates, prepared from the normal sulfates or chlorides by heating them with sulfuric acid [10], were dissolved in a slight excess of water and allowed to stand in a desiccator over phosphoric anhydride. The hydrosulfates crystallized out within 40-60 hours, the solutions gradually crystallizing completely. The crystals were kept in the desiccator until completely dried. Their weight corresponded exactly to the conversion of the original pyrosulfates into anhydrous hydrosulfates.

TABLE 1

Composition of Hydrosulfates Prepared by Evaporating Pyrosulfate Solutions

Compound	% of SO_3	
	Experimental	Calculated
$LiHSO_4$.....	76.87	76.97
$NaHSO_4$....	66.58	66.68
$KHSO_4$......	58.74	58.81
$RbHSO_4$.....	43.87	43.86
$CsHSO_4$.....	34.82	34.81

To check whether the hydrosulfates of the alkali elements produce hydrates with water under our experimental conditions, we re-treated the crystals with a small amount of water. The resulting solutions were set aside to crystallize in the air instead of in a desiccator over phosphoric anhydride, as in the first experiment. The crystals that settled out within 120-160 hours had their original weight. This proved that the hydrosulfates of the alkali elements we had prepared were anhydrous. The composition of the prepared hydrosulfates is given in Table 1. The analyses for SO_3 content were made by the usual gravimetric method, a weighed sample of the preparation being converted into barium sulfate.

The preparation of the anhydrous potassium hydrosulfate agrees with the observations made by Graham [11], but contradicts the researches of Montemartini [12] who believes that $KHSO_4$ crystallizes with one molecule of hydration water.

TABLE 2

Melting Points of Hydrosulfates of the Alkali Elements

Compound	M.p.
$LiHSO_4$.....	104±0.5°
$NaHSO_4$....	186
$KHSO_4$.....	216
$RbHSO_4$....	285
$CsHSO_4$....	110

The melting points of the hydrosulfates we had prepared were determined visually by heating a small portion of the substance in a capillary, using the device employed to measure the melting points of organic substances. The thermometer, with the capillary alongside it, was placed in the empty interior vessel of the device, without any vaseline. Tests showed that the convection air currents within the interior vessel transmit the temperature of the sulfuric acid in the outer vessel more quickly, thus ensuring more accurate determinations of the melting point. The thermometer was tested in advance at the melting point of ice and the boiling point of water. The melting points of the hydrosulfates, as established by a series of measurements, are listed in Table 2.

Lithium hydrosulfate melts at 160°, according to Schultz [3], and at 120°, according to Lescoeur [4]. Kendall and Landon [13] determined the melting points of sodium and potassium hydrosulfates as 186° and 218.6° respectively. Cambi and Bozza [14] give the melting point of sodium hydrosulfate as 185.7° and 213.8°, 214°, and 218° for potassium hydrosulfate. Older determinations of the potassium hydrosulfate melting point are 200° [15] and 210° [16].

The change in melting points in the alkali hydrosulfate series is typical of salts with an easily polarizable anion. The progressive rise in the melting point as we pass from lithium hydrosulfate to the hydrosulfates of sodium, potassium, and rubidium evidently depends upon a decrease in the polarizing action of the cations as their radii increase in size. The HSO_4^{-1} anion is perceptibly polarized apparently even when acted upon by a potassium ion. As we pass from the hydrosulfate of rubidium to the cesium salt, we observe a substantial drop of the melting point. This is most likely due to a decrease in the strength of the compound's crystal lattice, as a result of the large ionic radius of cesium.

When we compare these figures with those for the pyrosulfates [10], we should bear in mind that the potassium salt has the highest melting point among the latter, whereas the maximum melting point is shifted to the rubidium salt in the hydrosulfates. It is evident that the HSO_4^{-1} ion is more greatly deformed than the $S_2O_7^{-2}$ ion.

The hydrosulfates have melting points that average some 100-200° lower than the corresponding pyrosulfates. Their crystal lattices are not very strong, apparently because the HSO_4^{-1} ion is monovalent, while the $S_2O_7^{-2}$ ion is divalent. Moreover, the hypothetical high polarizability of the HSO_4^{-1} anion may likewise be a factor here.

One of the important properties of the hydrosulfates is their transformation into pyrosulfates at rather low temperatures, water being split out. According to Baum [17], "dark-red heat" is a prerequisite for this process, but the reaction takes place even at 260-320° when the preparation is heated at reduced pressure. According to Cambi and Bozza [14], sodium hydrosulfate slowly gives off water at approximately its melting point and is transformed into the pyrosulfate.

The thermal stability of the hydrosulfates was determined by taking samples of the latter (approximately 1 g), placing them in porcelain crucibles, and heating them in a drying cabinet, with the temperature raised gradually, until their weights remained constant.

TABLE 3

Heating Hydrosulfates of the Alkali Elements

Compound	Temp. at which the conversion to the pyrosulfate sets in	Yield of $Me_2S_2O_7$ from the $MeHSO_4$ (% of theoretical)	% SO_3 in the heating residue	
			Experimental	Calculated for the pyrosulfate
$LiHSO_4$...	90-100°	100.02	84.08	84.27
$NaHSO_4$..	140-150	99.70	72.07	72.09
$KHSO_4$....	160-170	100.00	62.89	62.96
$RbHSO_4$...	170-200	98.21	46.00	46.14
$CsHSO_4$...	150-180	99.94	36.18	36.23

The temperature at which the first loss of weight of at least 0.005 g was observed was taken as that at which the decomposition of the hydrosulfates sets in. In every case, the end product was a pyrosulfate, as shown by analysis. The temperatures at which the hydrosulfates are converted into pyrosulfates, and the percentages of SO_3 found in the resulting products are listed in Table 3.

According to Van Arkel and de Boor [18], cesium hydrosulfate is the most stable of the hydrosulfates of the alkali elements. Our findings indicate that its stability does not exceed that of rubidium hydrosulfate; on the contrary, it begins to decompose at a somewhat lower temperature. Only cesium hydrosulfate melts at a temperature that is lower than the point at which the salt begins to decompose. These temperatures practically coincide in the case of lithium hydrosulfate. It should be stated, however, that the hydrosulfates decompose extremely slowly at low temperatures. Cesium hydrosulfate, for example, begins to lose weight in the 150-180° range, but it has to be heated to 350° for 3-5 hours for decomposition (of a sample of about 2 g of the salt) to be complete. Thus, melting the salt rapidly produces no perceptible decomposition.

The low stability of the hydrosulfates, compared to the normal sulfates and the pyrosulfates must be attributed to the presence of the hydrogen ion in the hydrosulfate anion. The hydrogen ion, whose effective radius is small, penetrates the electronic shell of the anion and causes strong one-sided polarization of the latter, resulting in a relative decrease in the stability of the compound.

The polarizing action of the cation linked to the anion results in the phenomenon of counterpolarization, diminishing the stability of the compound. In the case of the hydrosulfates of the alkali elements, there is no doubt that the predominant factor influencing their stability is the decrease in the polarizing effect of the alkali element cation, due to the increasing radius as we pass from lithium to rubidium. This increases the compounds' stability and raises the temperature at which decomposition sets in as we travel along the series.

The somewhat lower stability of cesium hydrosulfate than that of rubidium sulfate may be due to the substantial polarizability of the cesium ion itself. The resulting reinforcement of the bond between the cesium and the oxygen atoms in the HSO_4^{-1} anion may weaken the bond of the latter's hydrogen atom and facilitate the splitting out of water. A related thermal decomposition of certain oxyacids has been described by one of the present authors [19] in the case of rubidium and cesium wolframates.

SUMMARY

1. The hydrosulfates of all the alkali elements have been prepared by evaporating aqueous solutions of their pyrosulfates to dryness at room temperature. This yields crystalline anhydrous hydrosulfates.

2. The melting points of the resulting compounds have been determined. Rubidium hydrosulfate has the highest melting point (285°). The melting points drop as we pass to the hydrosulfates of potassium (216°), sodium (186°), and lithium (104°), though cesium hydrosulfate's melting point is likewise low (110°).

3. The temperatures at which the hydrosulfates of the alkali elements begin to be transformed into pyrosulfates have been established. Rubidium hydrosulfate is the most stable (decomposition setting in at 170-200°). The stability of the hydrosulfates diminishes as we pass to potassium, sodium, and lithium (the temperatures at which decomposition sets in being 160-170°, 140-150°, and 90-100°, respectively). Cesium hydrosulfate decomposes somewhat more readily than rubidium hydrosulfate (150-180°).

4. The behavior patterns involved in the changes of the melting point and of the thermal stability of the hydrosulfates of the alkali elements have been discussed from the standpoint of concepts of polarizing action and polarizability of ions.

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Received October 9, 1950

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RESEARCH ON THE PYROSULFATES OF THE ALKALI ELEMENTS

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The applications of sodium and potassium pyrosulfates are of considerable importance in analytical chemistry and chemical technology. They are employed to decompose certain rare-earth and earth-acid minerals, such as euxenite, samarskite, tantalite, and the like, and to convert some oxides that are only slightly soluble in acids, such as Al_2O_3, Fe_2O_3, TiO_2, and the like, into salts.

The chemical action of these pyrosulfates is based upon the fact that they decompose, giving off sulfur trioxide, at temperatures above the boiling point of sulfuric acid and hence cause strong sulfatizing action.

Comparatively little research has been done as yet upon the pyrosulfates. There are no dependable data on their melting points and decomposition temperatures, while for some of the alkali elements there are no descriptions of the properties of their pyrosulfates.

We have prepared the pyrosulfates of all the alkali elements, measured their melting points and determined the temperatures at which they begin to be converted into the normal sulfates when calcined under various conditions (in air, in the presence of ammonium carbonate, in a current of ammonia, and in a current of hydrogen).

Flood and Ferland [1] produced lithium pyrosulfate by heating normal lithium sulfate to about 300° in an atmosphere of sulfur trioxide.

Weber [2] states that sodium and potassium pyrosulfates, of the $Me_2S_2O_7$ type, can be produced by reacting the thoroughly dried normal sulfates with sulfur trioxide in a sealed tube, heating the former to 150° and the latter to the temperature of a water bath. The same author asserts that normal rubidium and cesium sulfates react with sulfur trioxide to form the compounds $Rb_2O \cdot 8SO_3 (Rb_2S_8O_{25})$ and $Cs_2O \cdot 8SO_3 (Cs_2S_8O_{25})$, respectively, which readily give off 6 molecules of sulfur trioxide when heated, yielding the usual pyrosulfates.

According to Cambi and Bozza [3], sodium pyrosulfate is produced by reacting the sulfate with sulfur trioxide at 450°, the temperature required for potassium pyrosulfate being 470°.

Browning [4] states that when salts of the alkali elements and volatile acids are treated with an excess of sulfuric acid and heated to constant weight at 250-270°, they yield the hydrosulfate and pyrosulfate of lithium, pyrosulfates of the $Me_2S_2O_7$ type of sodium and potassium, and the $MeHSO_4$ hydrosulfates of rubidium and cesium.

TABLE 1

Analysis of Preparations of Pyrosulfates of the Alkali Elements

Compound	% SO_3	
	Experimental	Calculated
$Li_2S_2O_7$	84.16	84.27
$Na_2S_2O_7$	71.98	72.09
$K_2S_2O_7$	62.90	62.96
$Rb_2S_2O_7$	46.14	46.14
$Cs_2S_2O_7$	36.24	36.23

According to Erdmann [5], rubidium pyrosulfate can be produced by dissolving a rubidium salt with a volatile acid in an excess of sulfuric acid, then evaporating the solution in a platinum cup, and heating the resulting hydrosulfate.

We have produced the pyrosulfates by reacting sulfuric acid with the normal sulfates or chlorides of the alkali elements.

Lithium pyrosulfate was produced by treating the normal sulfate with the calculated quantity of dilute sulfuric acid. The mixture was evaporated on a water bath to drive off the excess water and then heated to 220° until the reaction was complete. The pyrosulfates of sodium and potassium were prepared by treating the normal sulfates with concentrated sulfuric acid and then heating the mixtures until the reactions were complete, the temperature required being 270° for sodium and 370° for potassium.

Rubidium pyrosulfate was prepared by heating a mixture of the chloride with a 20% excess of sulfuric acid, the temperature being gradually raised to 400°, until the weight remained constant.

TABLE 2

Melting Points of Pyrosulfates of the Alkali Elements

Compound	M.p.
$Li_2S_2O_7$.....	205±2°
$Na_2S_2O_7$....	402
$K_2S_2O_7$.....	440
$Rb_2S_2O_7$....	401
$Cs_2S_2O_7$....	280

Cesium pyrosulfate was produced by treating the normal sulfate or chloride with concentrated sulfuric acid. When the sulfate was used, the reaction mass was heated for 6.5 hours, the temperature being gradually raised to 500°, until the weight remained constant; with the chloride, heating lasted 18 hours, with the temperature raised to 370°.

The resulting preparations were analyzed in the usual manner, the SO_3 content being determined as $BaSO_4$. The results are listed in Table 1.

There are only a few figures given in the literature for the melting points of the pyrosulfates. Cambi and Bozza [3] found the melting point of sodium pyrosulfate to be 400.9°. Schultz-Sellack [6] states that potassium pyrosulfate melts far above 300°. We determined the melting points of our preparations by means of a platinum–platinum-rhodium thermocouple, from the cooling curves. The results of our measurements are given in Table 2.

The melting points are progressively higher in the series of lithium, sodium, and potassium salts. The potassium pyrosulfate has the highest melting point of all the compounds tested. The melting points drop off appreciably as we pass on to the rubidium and cesium salts. The general pattern of changes in the melting points of the pyrosulfates recalls the analogous picture in the iodides of the alkali elements. Here again, the readily polarizable $S_2O_7^{-2}$ anion is polarized by the sodium ion and more strongly so by the lithium ion, thus lowering the melting point as the ionic radius of the cation is diminished. This sort of polarizing action no longer exists, obviously, in the pyrosulfates of potassium, rubidium, and cesium. The successive drop of the melting points in this series of compounds must be due to the decrease in the stability of their crystal lattices as the ionic radii of the cations increase.

TABLE 3

Hygroscopicity of Pyrosulfates of the Alkali Elements

Compound	Time in air, hours	Mean hourly gain in weight, %
$Li_2S_2O_7$...	150	0.51
$Na_2S_2O_7$...	140	0.15
$K_2S_2O_7$...	140	0.02
$Rb_2S_2O_7$...	24	None
$Cs_2S_2O_7$...	115	0.007

We have found the pyrosulfates of the alkali elements to be more or less hygroscopic, with the sole exception of rubidium pyrosulfate. After these compounds had been exposed to the air for a long time, they exhibited the gains in weight set forth in Table 3.

The hygroscopicity of the pyrosulfates diminishes progressively from lithium to potassium; it is not present in rubidium, but reappears slightly in cesium. It is probable that this change in hygroscopicity is not fortuitous, but reflects the feasibility of adding water and of the ensuing hydrolysis of the compounds, depending upon the ionic radius of the alkali element and, he hence, the strength of the base formed by the given salt. The slight hygroscopicity of the cesium pyrosulfate may be due to the innate polarizability of the cesium ion when acted upon by the dipole of the water molecule that penetrates into the crystal lattice of the pyrosulfate.

TABLE 4

Temperatures at Which the Pyrosulfates of the Alkali Elements Begin to Change into the Normal Sulfates when Heated in Air

Compound	Temp. at which the pyrosulfate begins to change into the normal sulfate
$Li_2S_2O_7$....	200-220°
$Na_2S_2O_7$...	320-370
$K_2S_2O_7$....	370-420
$Rb_2S_2O_7$....	400-450
$Cs_2S_2O_7$....	500-520

The pyrosulfates' hygroscopicity must be allowed for whenever they are utilized.

We possess the following information on the temperatures at which the pyrosulfates are converted into normal sulfates. Cambi and Bozza [3] state that sodium pyrosulfate is converted into the normal sulfate at "red heat." At "red heat" rubidium pyrosulfate merely gives off some sulfur trioxide, being fully converted into the normal sulfate when the temperature is raised still further.

Flood and Ferland [1] investigated the thermal dissociation of some pyrosulfates in an atmosphere of sulfur trioxide at pressures of 1 to 0.4 atm. These authors found that the stability of the pyrosulfates rose progressively in the following series Ag–Li–Na and Tl–K. The systems of the normal sulfate and the pyrosulfate were investigated in various temperature ranges:

$Li_2SO_4-Li_2S_2O_7$	371-427°
$Na_2SO_4-Na_2S_2O_7$	555-655°
$K_2SO_4-K_2S_2O_7$	653-727°

We have investigated the temperatures at which the transition of the pyrosulfates to normal sulfates sets in when they are heated in air. Samples of the preparation, weighing 0.8-1 g approximately, were heated in porcelain crucibles in an electric furnace to constant weight, the temperature being gradually raised and the weight being checked at intervals. The temperature at which the first loss of weight amounting to at least 0.005 g was taken to be the temperature at which the pyrosulfate begins to decompose.

The SO_3 content of the end products corresponded to that in the normal sulfates.

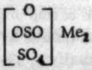
The temperatures at which we found the pyrosulfates beginning to change into the normal sulfates are listed in Table 4.

It should be noted that sulfur trioxide begins to split out of the pyrosulfates of sodium and potassium at temperatures that are about 50° below their melting points. This process is a time-governed one, however, a rather long heating period being required for complete decomposition. Thus, melting the salt rapidly does not entail any perceptible decomposition.

The pyrosulfates of lithium and rubidium break down immediately after these compounds are fused. Cesium pyrosulfate begins to decompose far above its melting point.

The rate at which the pyrosulfates are converted into the normal sulfates is indicated by the fact that in cesium pyrosulfate, for example, the decomposition reaction sets in slowly at 500-520°, becomes more intensive at 550-570°, and is completed only at 600°. The complete transformation of the sample used (0.8 g) into the normal sulfate required heating for a total of 18 hours.

When we compare the temperatures at which the various pyrosulfates begin to change into the normal sulfates, we find that the thermal stability of the pyrosulfates of the alkali elements increases progressively from lithium to cesium. Apparently, as the ionic radius of the cation increases in size, the polarizing effect of the latter, which is located in the outer sphere of the coordination compound:



$$\left[\begin{matrix}O\\OSO\\SO_4\end{matrix}\right]Me_2$$

upon the anion progressively diminishes resulting in an increase in the stability of the pyrosulfates. This pattern of behavior conforms to the well-known general rules governing the manner in which the stability of coordination compounds depends upon the properties of the cation in the second sphere of these compounds [7].

The fact that the thermal stability of the pyrosulfate is less than that of the normal sulfates [8] may be attributed to the presence of an appreciable counterpolarization effect in the anion due to the presence of a second sulfur ion. As has been stated above, rubidium and cesium compounds of the $Me_2O \cdot 8SO_3(Me_2S_8O_{25})$ type, i.e., containing even more sulfur atoms in the anion, are extremely unstable, being readily converted into the ordinary pyrosulfates when heated.

As indicated in the literature, the transformation of pyrosulfates into the normal sulfates by the application of heat is facilitated by the addition of ammonium carbonate. In the analytical determination of potassium as its normal sulfate, for example, ammonium carbonate is employed to decompose the $K_2S_2O_7$ mixed with the K_2SO_4 – "if solid ammonium carbonate is added, the SO_3 is converted into ammonium sulfate, which is highly volatile and can be eliminated at a lower temperature without any loss of potassium" [9]. We ran experiments on the effect of ammonium carbonate upon the stability of the pyrosulfates of all the alkali elements to check the correctness of these instructions.

As is seen from the figures in Table 5, we found that when the pyrosulfates of the alkali elements, with the sole exception of rubidium pyrosulfate, are heated with ammonium carbonate, they actually do change into the normal sulfates at lower temperatures. The effect is not too great, however. The addition of ammonium carbonate produces a drop of 30-50° in the temperature at which the pyrosulfates begin to decompose, the drop attaining 100° only in the case of cesium pyrosulfate.

References in the literature also state that the conversion of hydrosulfates, and hence of the pyrosulfates, of the alkali elements into the normal sulfates is accelerated in a current of ammonia. Hinrichsen and Sachsel [10], for example, recommend that rubidium pyrosulfate be calcined in a current of NH_3 to prepare the normal sulfate.

A sample of the pyrosulfate was placed in a porcelain boat and brought to constant weight at 700-750° in a current of ammonia, then placed within another protective boat and inserted into the porcelain tube of an electric furnace whose temperature was gradually raised. When the required temperature was attained, a current of dry ammonia was passed through the tube at the rate of 6 liters per hour.

TABLE 5

Effect of Adding Ammonium Carbonate Upon the Temperature at Which Pyrosulfates Begin to Change into Normal Sulfates

Compound	Temperatures at which pyrosulfates begin to change into normal sulfates	
	With $(NH_4)_2CO_3$	Without $(NH_4)_2CO_3$
$Li_2S_2O_7$....	170-220°	200-220°
$Na_2S_2O_7$....	270-320	320-370
$K_2S_2O_7$.....	320-370	370-420
$Rb_2S_2O_7$....	400-450	400-450
$Cs_2S_2O_7$....	400-420	500-520

After heating was over, the pyrosulfate was cooled in a current of air that had been previously dried in wash bottles containing sulfuric acid and in towers filled with phosphoric anhydride.

Our first experiments on heating lithium pyrosulfate in a current of ammonia showed that its conversion into the normal sulfate was a complicated process. At first, its weight increases due to the addition of ammonia to the pyrosulfate and the formation of an intermediate compound, which is transformed into the normal sulfate as the temperature continues to rise.

We found that ammonia is added even at room temperature (20-25°), the time required for this process being proportional to the amount of pyrosulfate.

Heating the intermediate product in a current of ammonia for an hour at 120, 170, and 220° showed that the product is thermally stable in this interval as well. The behavior of the product was investigated in a current of dry air at the same temperatures. No changes were observed.

TABLE 6

% of NH_3 in the Product of the Reaction of Lithium Pyrosulfate with Gaseous Ammonia

Weight of sample, g	Ammonia found	
	g	%
0.0820	0.0067	8.17
0.0758	0.0062	8.18
0.0750	0.0062	8.27
	Average	8.21

Our hygroscopicity investigations yielded positive results. The product absorbs hygroscopic moisture, which is then given off in the current of dry air even at room temperature.

These latter observations compelled us to suppose that the substance produced by the action of gaseous ammonia upon lithium pyrosulfate was a definite chemical compound rather than a product of the adsorption of ammonia on the lithium pyrosulfate. The percentage of ammonia was determined in three samples of the preparation in order to establish the composition of this compound.

The results are given in Table 6.

The compound $Li_2S_2O_7 \cdot NH_3$ has 8.21% of ammonia. When the temperature is raised above 220°, the $Li_2S_2O_7 \cdot NH_3$ begins to give up its ammonia and then its SO_3, being transformed into the normal sulfate.

TABLE 7

Comparison of the Temperatures at Which the Pyrosulfates of the Alkali Elements are Converted into the Normal Sulfates when Heated in Currents of Ammonia and of Air

Compound	Temperatures at which pyrosulfates begin to change into normal sulfates	
	In a current of ammonia	In air
$Li_2S_2O_7$...	220-270°	200-220°
$Na_2S_2O_7$...	320-370	320-370
$K_2S_2O_7$...	370-420	370-420
$Rb_2S_2O_7$...	Converted to a sulfide	400-450
$Cs_2S_2O_7$...	370-420	500-520

Our efforts to secure analogous ammonia addition products of the pyrosulfates of the other alkali elements at room temperature or after heating all met with failure. When heated, the pyrosulfates of sodium, potassium, and cesium were converted into the normal sulfates, while the rubidium pyrosulfate was converted into the sulfide.

The temperatures at which the pyrosulfates begin to change into normal sulfates when heated in a current of ammonia are listed in Table 7.

We see from Table 7 that heating in ammonia has no perceptible effect upon the temperature at which the pyrosulfates of sodium and potassium are converted into the normal sulfates, compared to their heating in air.

Only in the case of the cesium pyrosulfate did we find the conversion temperature lowered by 100-150°. The higher temperature at which lithium pyrosulfate is converted into the normal sulfate, as compared with its heating in air, does not apply to the $Li_2S_2O_7$, but rather to its ammonia compound, $Li_2S_2O_7 \cdot NH_3$.

The singular behavior of rubidium pyrosulfate is worthy of note, it being reduced by the ammonia to the sulfide, beginning at 300-350°. At 700° the reduction product is completely volatilized.

We also ran experiments to ascertain the behavior of the pyrosulfates of the alkali elements when heated in a current of hydrogen.

TABLE 8

Comparison of the Temperatures at Which the Pyrosulfates of Alkali Elements are Converted into Normal Sulfates when Heated in Currents of Hydrogen and of Ammonia

Compound	Temperatures at which pyrosulfates are converted into normal sulfates	
	In a current of hydrogen	In a current of ammonia
$Li_2S_2O_7$...	170-220°	220-270°
$Na_2S_2O_7$...	270-320	320-370
$K_2S_2O_7$....	370-420	370-420
$Rb_2S_2O_7$...	Converted to a sulfide	Converted to a sulfide
$Cs_2S_2O_7$...	470-520	370-420

As we see from Table 8, heating in a current of hydrogen lowers the temperature at which lithium and sodium pyrosulfates are converted into their normal sulfates, compared with heating in a current of ammonia. The temperature at which the potassium pyrosulfate was converted proved to be the same in both cases, whereas the cesium pyrosulfate was converted into the normal sulfate at a higher temperature. As in the current of ammonia, the rubidium pyrosulfate yielded a sulfide.

In conclusion, we should like to state that none of the various methods of accelerating the decomposition of the pyrosulfates utilized by us yielded substantial results. The principal factor determining the rate at which a pyrosulfate is converted into a normal sulfate is the temperature. The temperatures at which the decomposition reactions of the pyrosulfates set in fix the limits within which these compounds can be heated without losing sulfur trioxide. Utilizing temperatures that are 150-200° higher makes it possible to effect rapid decomposition of the pyrosulfates.

SUMMARY

1. The pyrosulfates of all the alkali elements have been produced, their melting points measured, and the temperatures at which they begin to change into normal sulfates determined under various conditions.

2. The melting points of the pyrosulfates rise progressively from lithium (205°) through sodium (402°) to potassium (440°), after which they drop off to rubidium (401.5°) and cesium (280°).

3. The thermal stability of the pyrosulfates rises progressively from lithium to cesium. The temperature at which $Li_2S_2O_7$ begins to decompose is 200-220°, and $Cs_2S_2O_7$ is 500-520°. The pattern of changes in stability of the pyrosulfates is discussed from the standpoint of concepts of the polarizing action of ions.

4. Adding ammonium carbonate merely lowers the decomposition temperature of the pyrosulfates negligibly. This additive has no effect upon rubidium pyrosulfate.

5. Heating cesium pyrosulfate in a current of ammonia accelerates its decomposition noticeably. Under these conditions the pyrosulfate of rubidium is converted into its sulfide. The temperatures at which decomposition sets in are not affected by ammonia in the other pyrosulfates.

6. Heating rubidium pyrosulfate in a current of hydrogen results in formation of a sulfide. Heating in a current of hydrogen has no substantial effect upon the temperature at which the pyrosulfates of the other alkali elements begin to decompose.

7. It has been found that lithium pyrosulfate forms the addition product $Li_2S_2O_7 \cdot NH_3$, in a current of ammonia. The thermal stability of this compound has been investigated.

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Received October 9, 1950

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THE ACTION OF LITHIUM HALIDES UPON ESTERS OF PHOSPHOROUS ACID

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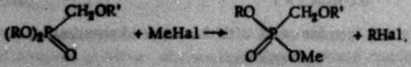
There are no researches on the action of halides of the alkali elements upon esters of phosphorous acid.

We have previously [1] investigated the action of the halides of the alkali elements sodium, potassium, and lithium upon the esters of alkoxymethylphosphinic acids, finding that heat caused the metal to replace one of the ester radicals, which was evolved as an alkyl halide. The overall equation may be written as follows:



By way of analogy with these reactions we made a study of the action of the lithium halides upon esters of phosphorous acid. We found that lithium halides do not react with phosphorous acid esters at ordinary temperature, though dissolution is violent when the mixture is heated. We succeeded in distilling an alkyl halide from the reaction products, the residue consisting of a lithium salt that proved to be a lithium dialkylphosphite upon analysis. The overall reaction may be written as:

$$(RO)_3P + LiBr \rightarrow (RO)_2POLi + RBr.$$

We reacted lithium bromide and chloride with the ethyl and butyl esters of phosphorous acid, obtaining lithium diethyl- and dibutylphosphite. Sodium iodide also acts upon esters of phosphorous acid, as has been demonstrated in preliminary tests.

The mechanism involved in these reactions must evidently be conceived of in this way: in the first stage the lithium halide is probably added to the phosphorus acid ester. This is borne out by analysis of the product secured by dissolving lithium bromide in triethylphosphite in a benzene medium, which contains 3% less phosphorus than lithium diethylphosphite, but much more than the addition product. The alkyl halide has split out during the ensuing stage.

EXPERIMENTAL

Action of lithium bromide upon the butyl ester of phosphorous acid. 1.74 g of lithium bromide was heated with 5 g of the butyl ester of phosphorous acid. The lithium bromide dissolved in the ester at 120°, with violent frothing. The heating lasted 30 minutes. Then butyl bromide (b.p. 98°; n_D^{20} 1.4312) was distilled from the reaction flask, the residue in the flask solidifying to a porous white mass. The salt was washed with absolute alcohol and dried in vacuum. The salt was a white powder that was insoluble in alcohol or ether, though soluble in water. The melting point of the salt was 456-460°, determined in a device using air heating.

Found %: P 15.58, 15.62. $C_8H_{18}O_3PLi$. Calculated %: P 15.50.

Action of lithium chloride upon the butyl ester of phosphoric acid. 0.68 gram of lithium chloride was heated in a flask with 4 g of the butyl ester of phosphorous acid. The lithium chloride dissolved in the ester at 120° with frothing. The distilled butyl chloride (b.p. 77°, n_D^{20} 1.4034) totaled 1.1 g or 74% of the theoretical. The residue was a white powder whose properties were the same as those described in the preceding experiment. M. p. 455-458°. The mixed melting point was 456-460°.

Action of lithium bromide upon the ethyl ester of phosphorous acid. 2.1 grams of lithium bromide was heated in a flask with 4 g of the ethyl ester of phosphorous acid in 20 ml of benzene. The lithium bromide dissolved after the mixture had been boiled for a long time. A white precipitate settled out when the mixture cooled. The benzene was decanted, and the residue was dried in vacuo on a water bath at 30-35°. The residue was a white powder that was insoluble in cold benzene, alcohol, or ether and soluble in water. The precipitate contained halogen.

Found %: P 18.17, 18.67. $C_6H_{15}O_3PLiBr$. Calculated %: P 12.25.

Then the residue was heated in vacuo to 100°. A Beilstein test of the residue was negative.

Found %: P 21.09, 21.20. $C_4H_{10}O_3PLi$. Calculated %: P 21.52.

Action of lithium chloride upon the ethyl ester of phosphorous acid. 1.02 grams of lithium chloride were heated to 200-210° for three hours in a sealed tube with 4 g of the ethyl ester of phosphorous acid. After the tube had been cooled, it contained a white precipitate, which was washed with ether. It is soluble in alcohol and ether.

Found %: P 21.02, 21.78. $C_4H_{10}O_3PLi$. Calculated %: P 21.52.

SUMMARY

It has been found that lithium chloride and bromide react with the esters of phosphorous acid, splitting out alkyl bromide and producing a lithium dialkylphosphite.

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Received October 11, 1950

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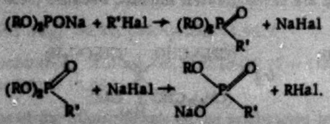
THE ACTION OF HALIDES OF THE ALKALI METALS UPON THE ESTERS OF ALKYLPHOSPHINIC ACIDS

V. S. Abramov and O. D. Samoilova

The action of alkyl halides upon acid salts is one of the methods of producing esters. In this reaction a halide is produced together with the ester. It is generally believed that this reaction proceeds to completion and cannot be reversed.

In some of our preceding papers [1] we have shown that sodium halides react with esters of alkylphosphinic acids to yield a mixed salt-ester of the alkylphosphinic acid and the alkyl halide. In this case we found a reverse reaction rather than in the formation of the esters. The action of sodium halides upon esters of alkylphosphinic acids was observed in our study of the reactions of alkyl halides with salts of dialkylphosphorous acids, which proceeded as follows:

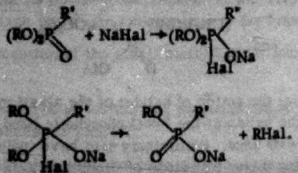


$$(RO)_2PONa + R'Hal \rightarrow (RO)_2P(=O)R' + NaHal$$

$$(RO)_2P(=O)R' + NaHal \rightarrow (RO)(NaO)P(=O)R' + RHal.$$

The sodium halide produced during the first stage of the reaction is not separated from the reaction products, the reaction mass being heated. This course of the reaction cannot be regarded as a universal one, however. Only those esters of alkoxymethylphosphinic acids or, generally speaking, esters of alkylphosphinic acids, the alkyl of which contains a polar group, react with sodium halides to yield mixed salt-esters. The nature of the alkyl group likewise affects the course of this reaction. It has not been possible as yet to establish any definite pattern of behavior in these reactions, however, owing to the lack of sufficient experimental data.

A mechanism had been proposed by V. S. Abramov and E. A. Miletskova [2] for the course taken by these reactions: the sodium halide being added at the P=O bond and then the alkyl halide split off:



$$(RO)_2P(R')=O + NaHal \rightarrow (RO)_2P(R')(Hal)ONa$$

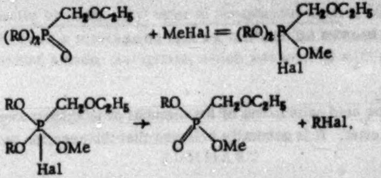
$$(RO)_2P(R')(Hal)ONa \rightarrow (RO)P(R')(=O)ONa + RHal.$$

Up to the present reactions of this sort have been observed only in the action of an alkyl halide upon a sodium dialkylphosphite, with subsequent distillation of the reaction products from the reaction mixture. The sodium halide formed when the reaction is carried out in anhydrous ether is highly disperse or, more accurately speaking, is colloidal in its nature, reacting with the pure esters of the alkylphosphinic acids when it is recovered from the reaction.

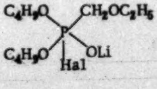
The present paper sets forth the results of reacting halides of the alkali metals with esters of alkylphosphinic acids. The objective of the research was determination of how the formation of mixed salt-esters of alkylphosphinic acids was affected by the nature of the metal and the halogen.

In our study of the action of halides upon esters of alkylphosphinic acids we prepared the butyl ester of ethoxymethylphosphinic acid, the butyl ester of ethyl phosphonacetate, and the isopropyl ester of ethoxymethylphosphinic acid. These esters were prepared by reacting bromomethyl ethyl ether with the butyl and isopropyl esters of phosphorous acid, respectively, and reacting ethyl bromoacetate with butyl ester of phosphorous acid.

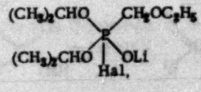
We investigated the action of sodium, potassium, and lithium chlorides, bromides, and iodides upon these esters of the alkylphosphinic acids. We found that the ordinary crystalline halides of the alkali metals react with esters of alkylphosphinic acid, yielding mixed salt-esters as follows:



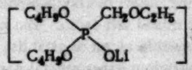
This pattern of the action of the halides is founded solely upon the properties of the reagents and of the end products. We have not secured a direct proof that the reaction actually follows this course. Isolation of the intermediate product of the addition of the halide to the ester of the alkylphosphinic acid would constitute direct proof of the reaction mechanism. In this respect, the action of lithium halides upon the butyl and isopropyl esters of ethoxymethylphosphinic acid are of the greatest interest, because these reactions yield addition products whose composition is:



and



where Hal = chlorine, bromine, and iodine. The structure of the resultant products may also be represented as that of phosphonium salts:



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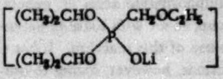
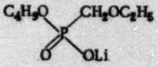


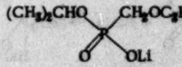
Hal.

which requires further study and proof, however.

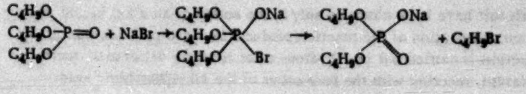
When the addition products are heated, the alkyl halide splits out, and the products are converted into the following mixed salt-esters of ethoxymethylphosphinic acid:



and



This suggested (and confirmed) mechanism for the action of halides of the alkali metals upon the esters of alkylphosphinic acids, involving the addition of the halide at the P=O phosphoric bond, raised the question of the action of halides upon esters that contain a P=O bond. Preliminary tests have indicated that butyl phosphate reacts with sodium bromide and iodide, yielding mixed salt-esters of phosphoric acid as follows:



EXPERIMENTAL

Synthesis of the butyl ester of ethyl phosphonacetate. 28.5 grams of butyl phosphite was placed in a flask fitted with a reflux condenser, and 19 g of ethyl bromoacetate was added. After all the ester had been added, the reaction products were refluxed for one hour at 60° and then fractionated at ordinary pressure. At 100° 9 g (60% of the theoretical) of butyl bromide with n_D^{20} 1.4375 (1.4398 in the literature) was distilled off, the residue yielding (after two consecutive fractionations in vacuo) the butyl ester of ethyl phosphonacetate, with a b.p. of 182-182.5° at 16 mm. The ester yield was 1 g, or 65% of the theoretical.

n_D^{20} 1.4340; d_4^{20} 1.043; MR_D 69.65; calculated 69.27.

0.2260 g, 0.2032 g substance: 49.3, 45.4 ml NaOH (T = 0.01779). Found %: P 10.74, 11.02. $C_{12}H_{25}O_5P$. Calculated %: P 11.05.

Synthesis of the butyl ester of ethoxymethylphosphinic acid. 25 grams of monobromomethyl ethyl ether was added to 45 g of butyl phosphite, heat being evolved as addition took place. The reaction was completed by heating the reaction mixture to 150-160° for 1.5 hours. The reaction products were then fractionated. 18 grams (or 73% of the theoretical) of butyl bromide (n_D^{20} 1.4370), was driven off at 100° and atmospheric pressure. Two successive frationations of the residue yielded the butyl ester of ethoxymethylphosphinic acid, with a b.p. of 143-143.5° at 10 mm. The ester yield was 35 g, or 77% of the theoretical.

n_D^{20} 1.4380; d_4^{20} 0.998; MR_D 64.67; calculated 64.81.

0.2160 g, 0.2556 g substance: 53.88 ml, 65.5 ml NaOH (T = 0.01779). Found %: P 12.28, 12.61. $C_{11}H_{25}O_4P$. Calculated%: P 12.3.

Synthesis of the isopropyl ester of ethoxymethylphosphinic acid. The isopropyl ester of ethoxymethylphosphinic acid was synthesized, like the butyl ester, from 35 g of isopropyl phosphite and 23 g of monobromo methyl ethyl ether. We secured 11.5 g, or 55% of the theoretical, of isopropyl bromide, with a b.p. of 59-60°. The yield of the isopropyl ester of ethoxymethylphosphinic acid, with a b.p. of 107.5-108° at 8 mm, was 23 g or 60% of the theoretical.

n_D^{20} 1.4195; d_4^{20} 1.007; MR_D 56.24; calculated: 55.44.

0.2600 g, 0.1427 g substance: 64.0 ml, 36.1 ml NaOH (T = 0.02094). Found %: P 13.55, 14.0. $C_9H_{21}O_4P$. Calculated %: P 13.80.

Action of the halides of the alkali metals on the synthesized esters of phosphinic acids. The reaction was carried out in a two-necked flask so designed that one mouth was stoppered by a hollow, ground-glass stopper containing a capillary, while the other was stoppered with a reflux condenser, which we could convert into a straight condenser by turning it upside down. This setup enabled us to drive off the liquid products after the reaction was complete without taking the apparatus apart.

An equimolecular quantity of the alkali metal halide was added to the ester of phosphinic acid. The reaction products were then refluxed until the salt dissolved. Then the straight condenser was employed to drive off the alkyl halide, which was identified by its boiling point and refractive index. What was left as a residue was a mixed salt-ester of the alkylphosphinic acid, which was washed with alcohol or recrystallized from alcohol and analyzed for its phosphorous content. It was very hard to purify the salt-ester, however, so that the phosphorus percentage found was sometimes very far from the theoretical percentage.

The results of the reaction of the alkali metal halides with the butyl ester of ethyl phosphonacetate are listed in Table 1.

The results of the reaction of sodium and potassium halides with the butyl ester of ethoxymethylphosphinic acid are summarized in Table 2.

Action of lithium chloride upon the dibutyl ester of ethoxymethylphosphinic acid. When 0.33 g of lithium chloride was heated to 105° with 2 g of the butyl ester of ethoxymethylphosphinic acid, the lithium chloride dissolved and the reagents reacted together. Part of the lithium chloride did not enter into the reaction. The compound that was produced did not dissolve in organic solvents and therefore was not purified.

Analysis of the crude product for phosphorus gave the following results:

Found %: P 6.9, 7.0, 6.72. $C_7H_{16}O_4PLi$. Calculated %: P 15.35. $C_{11}H_{25}O_4P$. Calculated %: P 10.72.

We evidently secured an addition product that contained part of the unreacted lithium chloride. The unreacted ester of the phosphinic acid was eliminated by washing the product with alcohol.

Action of lithium bromide upon the dibutyl ester of ethoxymethylphosphinic acid. When 0.69 g of lithium bromide was heated to 60-75° with 2 g of the butyl ester of ethoxymethylphosphinic acid, dissolution was complete and the lithium bromide reacted with the ester. The product crystallized when it was chilled with snow. The melting point of the crystals was 92-94°.

TABLE 1

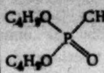
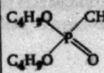
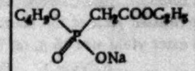
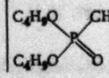
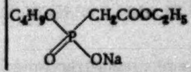
No.	Halide	Ester of Phosphinic acid	Heating temperature	Product obtained	Analysis for P, % Calculated	Analysis for P, % Experimental	Remarks
1	NaCl		210-230°	Does not react	—	—	
2	NaBr		190-200		12.6	12.78, 12.76	The salt dissolved in alcohol, precipitating the ester
3	NaI		210-220		12.6	12.08, 12.45	

TABLE 2

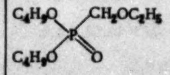
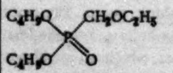
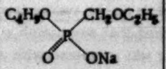
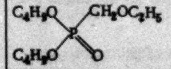
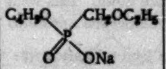
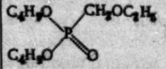
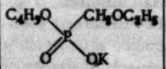
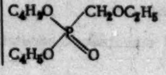
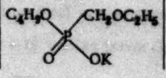
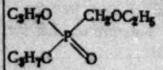
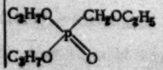
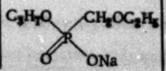
No.	Halide	Ester of Phosphinic acid	Heating temperature	Product obtained	Analysis for P,% Calc.	Analysis for P,% Experi.	Distillation temperature	Isolated alkyl halide Boiling pt	Isolated alkyl halide n_D^{20}
1	NaCl		210-220°	Does not react	—	—	—	—	—
2	NaBr		200-210		14.20	14.22, 13.97	220-230°	100°	1.4368
3	NaI		210-217		14.20	14.30, 13.98	220-230	128	1.4795
4	KBr		150-160		13.22	13.55, 13.10	200-210	100	1.4305
5	KI		150-160		13.22	12.70, 13.00	200-215	128	1.4795

TABLE 3

No.	Halide	Ester of Phosphinic acid	Heating temperature	Product obtained	Analysis for P,% Calc.	Analysis for P,% Experi.	Distillation temperature	Isolated alkyl halide Boiling pt.	Isolated alkyl halide n_D^{20}
1	NaCl		250°	Does not react	—	—	—	—	—
2	NaBr		180 - 190°		15.5	14.6, 14.9	200-210	57-58°	1.4202

0.1043 g, 0.1800 g substance: 16.4 ml, 26.9 ml NaOH (T = 0.02094). 0.1020 g substance: 0.0527 g AgBr. Found %: P 8.70, 8.25; Br 23.0. $C_{11}H_{23}O_4$ BrPLi. Calculated %: P 9.14; Br 23.55.

The addition product was heated to 150-160° in a flask attached to a straight condenser, butyl bromide with an b.p. of 98° and n_D^{20} 1.4348 being driven off. The flask residue solidified into a porous white mass. The salt-ester was insoluble in absolute alcohol.

0.0745 g. 0.1007 g substance: 20.1 ml 27.2 ml NaOH (T = 0.2094). Found %: P 14.85, 14.95. $C_7H_{16}O_4PLi$. Calculated %: P 15.35.

Action of lithium iodide upon the dibutyl ester of ethoxymethylphosphinic acid. When 1.2 g of lithium iodide was heated with 2 g of the butyl ester of ethoxymethylphosphinic acid, the iodide dissolved and the reagents reacted together. Dissolution also took place at room temperature. A small quantity of liquid was distilled off at 140°. The residue solidified into a reddish hyaline mass, which was ground to a powder and washed with alcohol.

0.1417 g. 0.1805 g substance, 27.0, 37.0 ml NaOH (T = 0.2094). Found %: P 9.37, 9.27. $C_{11}H_{25}O_4IPLi$. Calculated %: P 8.03. $C_7H_{16}O_4PLi$. Calculated %: P 15.35.

The results of the reaction of sodium halides with the diisopropyl ester of ethoxymethylphosphinic acid are summarized in Table 3.

Action of sodium iodide upon the diisopropyl ester of ethoxymethylphosphinic acid. When 1.34 g of sodium iodide and 2 g of the isopropyl ester of ethoxymethylphosphinic acid were heated together to 180°, they interacted and were transformed into a homogeneous mass, which hardened upon cooling. The mass had a reddish color and deliquesced when exposed to the air.

0.2710 g. 0.1326 g substance: 43.9, 22.3 ml, NaOH (T = 0.01998). Found %: P 8.91, 9.34. $C_9H_{21}O_4IPNa$. Calculated %: P 8.30.

Action of lithium chloride upon the diisopropyl ester of ethoxymethylphosphinic acid. When 0.38 g of lithium chloride and 2 g of the isopropyl ester of ethoxymethylphosphinic acid were heated together to 80-85°, the chloride dissolved and reacted, producing a homogeneous white mass. The reaction product was hygroscopic.

0.0792 g. 0.1560 g substance: 15.5 ml, 34.3 ml, NaOH (T = 0.01998). Found %: P 12.23, 12.16. $C_9H_{21}O_4ClPLi$. Calculated %: P 11.63.

The addition product was heated to 150-160° with a straight condenser. A liquid with a b.p. of 35-36°, the boiling point of isopropyl chloride, was distilled off. The residue was a white mass, which was washed with alcohol and analyzed.

0.0718 g. 0.0886 g substance: 21.1 ml, 25.75 ml NaOH (T - 0.01998). Found %: P 16.26, 16.07. $C_6H_{14}O_4PLi$. Calculated %: P 16.49.

Action of lithium bromide upon the diisopropyl ester of ethoxymethylphosphinic acid. When 1.6 g of lithium bromide was heated to 85-90° with 3 g of the isopropyl ester of ethoxymethylphosphinic acid the reagents interacted, yielding an addition product. The hyaline mass deliquesced in air.

0.2468 g. 0.2332 g substance: 47.0 ml, 43.0 ml NaOH (T - 0.2094). Found %: P 10.50. 10.02. $C_9H_{21}O_4BrPLi$. Calculated %: P 10.0

The addition product was heated to 180-190°. Isopropyl bromide, with a b.p. of 58-59°, n_D^{20} 1.4198, which agree with the figures in the literature, was distilled. The residue was a white porous mass, which was washed with absolute alcohol and analyzed.

0.0968 g. 0.1530 g substance: 28.5 ml, 43.9 ml NaOH (T = 0.02094). Found %: P 16.34, 15.9. $C_6H_{14}O_4PLi$. Calculated %: P 16.49.

Action of sodium bromide upon butyl phosphate Equimolecular quantities of sodium bromide and butyl phosphate were heated to 170-200°. We then distilled off a liquid product with a b.p. of 101°, which is that of butyl bromide. The residue in the flask solidified into a porous white mass. The residue was purified by dissolving it in absolute alcohol.

0.0736 g substance: 18.8 ml NaOH (T = 0.01779). Found %: P 12.58. $C_8H_{18}O_4PNa$. Calculated %: P 13.35.

SUMMARY

1. The halides of lithium, sodium, and potassium react with esters of alkyl-phosphinic acids whenever the alkyl radical contains a polar group, yielding salt-esters of these acids.

2. The velocity of the reaction of the halides with the esters of alkylphosphinic acids depends upon the nature of the metal, the halogen, and the ester radical.

3. The addition products of lithium chloride and bromide to esters of alkylphosphinic acids have been isolated, thus establishing the mechanism involved in these reactions.

4. Sodium halides react with butyl phosphate.

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[2] V. S. Abramov and E. A. Miletskova, J. Gen. Chem. 22, 252 (1952). See Consultants Bureau translation, p. 309.

Received October 11, 1950.

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THE REACTION OF SOME PHOSPHORUS HALIDES WITH ESTERS OF GLYCOLIC ACID

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The reaction of phosphorus halides with alcohols has been extensively investigated and is a matter of common knowledge. In particular, when phosphorus trichloride or tribromide is reacted with alcohols, we get satisfactory yields of neutral or acid esters of phosphorous acid, depending upon the conditions. As in the case of phosphorus trichloride, the reaction of other halogen compounds of phosphorus of the following types: $ArPCl_2$; Ar_2PCl; $(RO)PCl_2$; and to a lesser extent, of the $(RO)_2PCl$ type, has been investigated [1-7]. But alongside this, we have practically no knowledge of the reaction of the foregoing phosphorus halides with such hydroxyl compounds as the hydroxy acids, or, more precisely, their esters.

We know of only two brief references to such compounds in the existing literature. The paper by Cook, Saunders, and McCombie [8] gives an outline of the reaction between phosphorus trichloride and ethyl lactate, resulting in the production of di-(1-carbethoxyethyl)-phosphoric acid. The latter was then converted into the respective phenylamide of di-(1-carbethoxyethyl)-phosphoric acid by chlorinating it still further and then treating it with aniline. No other information is given, nor is any of the compounds identified. The other instance is that of Dietrich's patent, which mentions the production of the tricarbopropoxymethyl ester of phosphorous acid $P(OCH_2COOR)_3$. The ester is not identified in the patent, nor is any other information given [9].

We were interested in studying the reactions mentioned above, as well as the properties of the resulting compounds. We report the results of these investigations in the present paper.

The simplest representatives of the hydroxy acids were selected, namely the esters of glycolic acid. The halogen compounds of phosphorus employed were phosphorus trichloride, the alkoxydichlorophosphines $ROPCl_2$, and the dialkoxychlorophosphines $(RO)_2PCl$. We tried to synthesize a phosphite of the $P(OCH_2COOR)_3$ type by reacting an ester of glycolic acid with phosphorus trichloride and dimethylaniline in anhydrous ether.

$$PCl_3 + 3HOCH_2COOR + 3C_6H_5N(CH_3)_2 \rightarrow P(OCH_2COOR)_3 + 3C_6H_5N(CH_3)_2 \cdot HCl. \quad (1)$$

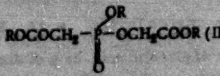
In our first experiment, run at 30-35°, we were able to recover substantial quanties of nothing but the respective ester of chloroacetic acid. Nor were we able to secure the desired product in the next experiment, in which chilling was employed, though we did get its isomerization product, namely: $ROCOCH_2-PO(OCH_2COOR)_2$ (I) the yield being 45% of the theoretical. As a compound of pentavalent phosphorus, it did not react with bromine or with monovalent copper salts. We have established the composition of the compound and its properties. The production of an isomerization product may be explained in different ways. As we know, such isomerization processes can be brought about by thermal causes, but we believe it is more likely that this process is due to the formation of an ester of chloroacetic acid in the reaction medium.

Reacting the ester of glycolic acid with the dialkoxychlorophosphine yielded a normal product as follows:

$$(RO)_2PCl + HOCH_2COOR + C_6H_5N(CH_3)_2 \rightarrow \underset{(II)}{(RO)_2POCH_2COOR} + C_6H_5N(CH_3)_2HCl. \quad (2)$$

Using a lower temperature for the reaction and a higher vacuum when fractionating the resultant mixture increases the yield of (II).

In addition to (II), we also secured the compound



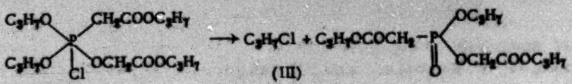
$$ROCOCH_2-\overset{OR}{\underset{O}{P}}-OCH_2COOR$$

(III).

The compound (III) formed in a so-called Arbuzov rearrangement, can be produced only when the reaction medium contains an ester of chloroacetic acid, as we have demonstrated.

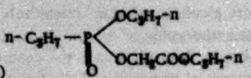
Compound (II) was processed under certain conditions with an ester of chloroacetic acid to provide more convincing proof of the structure of (III). As a compound with trivalent phosphorus, the compound (II) should enter into an Arbuzov rearrangement with the ester of chloroacetic acid, as follows:

$$(\text{n-}C_3H_7O)_2POCH_2COOC_3H_7\text{-n} + ClCH_2COOC_3H_7\text{-n} \rightarrow \qquad (3)$$



(III)

As a matter of fact, this product was isolated and its properties proved to be the same as those of (III). We also secured the compound (IV), in addition to the normal rearrangement product.



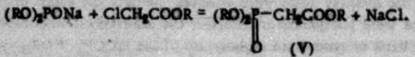
(IV)

The only explanation for the production of (IV) is the formation of propyl chloride during the reaction pictured in (3). This chloride evidently enters into "competition" with the ester of chloroacetic acid, resulting in the formation of (IV) by an analogous reaction (Schema 3).

We also synthesized the product (II) by another method in order to explore the conditions governing its formation and yield. By analogy with the A.E. Arbuzov method for alcoholates of alcohols [10], we prepared a metallic derivative of an ester of chloroacetic acid and then reacted it with dialkoxychlorophosphine in ether as follows:

$$(RO)_2PCl + NaOCH_2COOR \rightarrow (RO)_2POCH_2COOR + NaCl. \qquad (4)$$

Recovery of the substance requires repeated fractionation in this case as well, since a rather complex mixture is ordinarily produced in the reaction. The resulting substance has properties that are identical with those of (II), produced by the first method. As a compound with trivalent phosphorus, it reacts violently with bromine and also reacts with cuprous salts, though it does not constitute crystalline compounds. For the sake of comparing it with (II) we synthesized an isomeric compound with pentavalent phosphorus (V) in the following reaction:



$$(RO)_2PONa + ClCH_2COOR = (RO)_2\underset{\displaystyle O}{\overset{}{\underset{\|}{P}}}-CH_2COOR + NaCl. \qquad (5)$$

(V)

(V) differs pronouncedly from (II) and does not react with bromine, nor does it enter into reactions with cuprous salts.

We succeeded in securing a small quantity (about 10 g) of the normal reaction product, the composition of which was $C_2H_5O-P(OCH_2COOC_2H_5)_2$ (VI), by reacting ethyl glycolate with an alkoxydichlorophosphine. The composition and the purity of the isolated product were established by analysis and by its molar refraction. The product was subjected to an Arbuzov rearrangement by exposing it to the action of ethyl iodide, a very small quantity of the normal rearrangement product, $C_2H_5-PO(OCH_2COOC_2H_5)_2$ (VII), being recovered.

This research demonstrates that the ease with which chlorine can be substituted for a hydroxyl group and the formation of esters of chloroacetic acid both affect the course of the reaction. There is no doubt that chlorinating ability diminishes progressively in the following order: $PCl_3 \rightarrow ROCl_2 \rightarrow (RO)_2PCl$. It is therefore easier to secure a normal product with trivalent phosphorus by reacting an ester of glycolic acid with a dialkoxychlorophosphine, $(RO)_2PCl$; this procedure likewise gave us the highest yield. The yield of the product with an alkoxydichlorophosphine was much lower, while the reaction with phosphorus trichloride yielded nothing but a product in an isomeric state.

EXPERIMENTAL

Reaction of Phosphorus Trichloride with Ethyl Glycolate

1. 39 g of the ethyl ester of glycolic acid, 55 g of dimethylaniline, and anhydrous ether as a solvent were placed in a flask fitted with a stirrer, a reflux condenser and a thermometer, and the mixture was chilled with snow while 18 g of phosphorus trichloride was added. The temperature of the reaction mass was 30-32°. After all the phosphorus trichloride had been added, the mass was refluxed for 30 minutes, the ether boiling gently. The dimethylaniline hydrochloride was filtered out, the ether driven off, and the product fractionated. Red phosphorus settled out at a bath temperature of approximately 120°, and a liquid with a b.p. of 40-42° at 15 mm was distilled off, which proved to be ethyl chloroacetate.

2. 39 g of ethyl glycolate and 46 g of dimethylaniline were placed in the same type of flask as that used in the first test, and 17.5 g of phosphorus trichloride was added. Anhydrous ether was used as the solvent. The reaction was run at a temperature of −5 to −10°, in contrast to the first test, with fractionation performed at 0.5 mm vacuum. Triple fractionation yielded a fraction with a boiling point of 156-158° at 0.5 mm – a colorless liquid with a faint, characteristic odor. The yield was 18 g (43% of the theoretical). The product did not react with a cuprous halide, nor did it decolorize bromine. It reacted readily with metallic sodium.

d_4^{20} 1.2134; n_D^{20} 1.4405; MR_D 73.91; calculated 73.34.
0.1183 g substance: 18.70 ml NaOH. 0.1643 g substance: 27 ml NaOH (1 ml NaOH = 0.0005707 g P).
Found %: P 9.03, 9.37; $C_{12}H_{21}O_9P$. Calculated % P: 9.12.

Analysis indicated that the product was the compound (I).

Synthesis of dipropyl-(carbopropoxymethyl) phosphite. For the purposes of this synthesis we prepared di-n-propoxychlorophosphine by a method worked out in our laboratory [11,12], and the n-propyl ester of glycolic acid. The latter was prepared, in accordance with the references in the literature, from propyl chloroacetate and sodium glycolate [13]. We prepared the ester by reacting n-propyl alcohol with glycolic acid in the presence of sulfuric acid, using 5 g of sulfuric acid to 19 g of glycolic acid and 55 g of the alcohol. The mixture was refluxed for 6-7 hours, after which the sulfuric acid was neutralized with potash, and the precipitated potassium sulfate filtered out. The residual potassium salt was thrown down by adding ether and then refiltered out. This yielded 17 g (58% of the theoretical). B.p. 63.2-63.5° at 12 mm; d_4^0 1.0725; d_{18}^{18} 1.0563; n_D^{20} 1.4138. The ester was analyzed, because of the discrepancies in the physical constants cited in the literature. Found %: C 50.38; H 8.64; $C_5H_{10}O_3$. Calculated %: C 50.84; H 8.47. The analysis of the product and the steady boiling point are indisputable proof of the high purity of the product.

The ester was synthesized in the same vessel as that used in the preceding experiment. For the reaction we took 12.5 g of the n-propyl ester of glycolic acid and 13 g of dimethylaniline in anhydrous ether, chilling the mixture to −5 to −10°, and adding 19 g of dipropoxychlorophosphine diluted with anhydrous ether. Double fractionation yielded two fractions. Fraction 1 was a colorless liquid with the typical odor of a phosphite. B.p. 139-140° at 8 mm, 116-117° at 0.25 mm. It reacted violently with bromine. It entered into reaction with cuprous salts, evolving considerable heat, but no crystalline products were formed.

d_4^{20} 1.001; n_D^{20} 1.4267; MR_D 68.03; calculated 67.81.

0.2113 g substance: 45.8 ml NaOH. 0.1666 g substance: 36.6 ml NaOH (1 ml NaOH = 0.0005707 g P).
Found % P: 11.90, 11.83; $C_{11}H_{23}O_5P$. Calculated %: P 11.66.

Thus, its analysis, molar refraction, and properties all are evidence that this is the normal product (II). The product yield is increased by using a higher vacuum during fractionation, 9.3 g (27% of the theoretical) being obtained in the second experiment.

Fraction 2 was a colorless, nearly odorless liquid. B.p. 150-152° at 15 mm. It does not decolorize bromine nor does it react with a cuprous salt.

d_4^{20} 1.1051; n_D^{20} 1.4398; MR_D 76.90; calculated 76.40.
0.2097 g substance: 37.6 ml NaOH. 0.1852 g substance: 32.97 ml NaOH (1 ml NaOH = 0.0005707 g P).
Found %: P 10.16, 10.26. $C_{13}H_{25}O_7P$. Calculated %: P 9.56.

The analysis, molar refraction, and properties of this fraction indicate that it is the compound (III).

Rearrangement. 9 g of the phosphite (II) was placed in a sealed tube with 5 g of the n-propyl ester of glycolic acid and heated to 140° for 4 hours. This resulted in a considerable diminution of the liquid in the tube. The change in volume ceased after 5 hours, and heating was stopped. Two fractions were collected in vacuum fractionation.

Fraction 1 was a colorless, nearly odorless liquid, which did not react with bromine. It weighed 2 g (22% of the theoretical). B.p. 154-155° at 2.5 mm.

d_4^{20} 1.0627; n_D^{20} 1.4350; MR_D 65.36; calculated 65.32.

0.1164 g substance: 23.0 ml NaOH. 0 1450 g substance: 29.3 ml NaOH (1 ml NaOH = 0.0005707 g P).
Found %: P 11.29, 11.53. $C_{11}H_{25}O_5P$. Calculated %: P 11.66.

The analysis, molar refraction, and properties of this substance were those of the compound (IV).

Fraction 2 was a colorless, nearly odorless liquid, which did not react with bromine. The yield was 4 g (38% of the theoretical). B.p. 176-177° at 2.5 mm.

d_0^{20} 1.1059; n_D^{20} 1.4392.
0.1162 g substance: 19.57 ml NaOH (1 ml NaOH = 0.0005707 g P). Found %: P 9.56. $C_{13}H_{25}O_7P$.
Calculated %: P 9.56.

The analysis and the constants indicated that we had secured the normal rearrangement product (II).

Synthesis of dipropyl-(carbopropoxymethyl) phosphite via a metallic derivative of ethyl glycolate. An alcoholate was prepared from 4.7 g of sodium and 75-80 g of n-propyl alcohol, and 23.8 g of n-propyl glycolate was added to it. The alcohol was driven off, first at ordinary pressure, and then by the A.E.Arbuzov method; the sodium derivative "swelled up." It should be noted that this swelling is not as satisfactory as in the alcoholates of the simpler alcohols.

Anhydrous ether was added to the sodium derivative, and the mixture was stirred and chilled while 38 g of dipropoxychlorophosphine was gradually added. After all the phosphine had been added, the mass was heated for one hour; then the sodium chloride was filtered out, the solvent driven off, and the ester distilled in vacuo.

Triple fractionation yielded a fraction with a b.p. of 139-141° at 6 mm.

d_0^{8} 1.0492; $n_D^{20.5}$ 1.4261.
0.1135 g substance: 27.25 ml NaOH. 0.1374 g substance: 32.40 ml NaOH (T = 0.01848)
Found %: P 11.91, 11.70. $C_{11}H_{23}O_5P$. Calculated %: P 11.65.

It reacted actively with bromine like a trivalent phosphorus compound, 0.2 g of the ester using up 1.13 g of bromine (until the color was a light yellow). Theoretically 0.12 g of bromine was required. 0.5 g of the ester was mixed with 0.36 g of CuI (1:1). The mass warmed up considerably (45°), but yielded no crystalline product, a thick, colorless liquid being formed.

The analysis, physical constants, and behavior of this product indicate that it is the same as the compound (II) described above.

Synthesis of the ester (V). The ester was preparing by reacting the sodium derivative of dipropylphosphorous acid with n-propyl chloroacetate. We took 37.5 g of dipropylphosphorous acid, 7 g of metallic sodium, and 40.65 g of the chloroacetate for this reaction, which was carried out in a solution of anhydrous ether. Filtering out the sodium chloride and driving off the solvent yielded 70 g of the crude product (88% of the theoretical). Fractionation yielded the ester with a b.p. of 142.5-143° at 3 mm.

n_D^{20} 1.4279.

0.1311 g substance: 28.3 ml NaOH. 0.1373 g substance: 29.8 ml NaOH (T = 0.019946).
Found %: P 11.26, 11.32. $C_{11}H_{23}O_5P$. Calculated %: P 11.65

The ester behaves like a pentavalent phosphorus compound, turning dark red with a single small drop of bromine, and failing to react with a cuprous halide. The reaction with metallic sodium is vigorous.

Reaction of ethyl glycolate with ethoxydichlorophosphine. 48 g of ethyl glycolate, 73 g of dimethylaniline, and 500 ml of absolute ether were placed in a 1-liter three-necked flask, fitted with a reflux condenser, a stirrer, and a dropping funnel; the flask was chilled with a freezing mixture.

34 g of ethoxydichlorophosphine, diluted with anhydrous ether, was slowly added a drop at a time from the dropping funnel, the temperature within the reaction flask being kept at −10°. After the reaction was over, the dimethylaniline hydrochloride was eliminated and the solvent driven off. A large number of fractionations of the principal product, some of them performed with a Widmer column, yielded a fraction with a b.p. of 146° at 2.0 mm, the yield being 9.4 g, or 14.8% of the theoretical.

A colorless, highly mobile liquid with a peculiar odor, insoluble in water, and reacting violently with bromine.

d_0^{19} 1.1513; n_D^{19} 1.4412; MR_D 64.70; calculated 64.75.

0.1847 g substance: 32.8 ml NaOH. 0.1147 g substance: 21.2 ml NaOH(T = 0.0617). Found %: P 10.95, 10.40.
$C_{10}H_{19}O_7P$. Calculated %: P 10.99.

Rearrangement. 8 g of the synthesized ester was sealed into a tube together with 4.5 g of ethyl iodide and heated to 140° for 4 hours. The product discovered after the tube was opened had a dark color; the color was lightened by processing the product with activated charcoal, after which it was distilled. A fraction with a b.p. of 2.5 mm, totaling 0.5 g, was collected. A difficultly mobile liquid with a singular odor, which does not react with bromine.

0.1770 g substance: 23.9 ml NaOH. 0.1613 g substance: 26.9 ml NaOH (T = 0.0684). Found %: P 11.32. $C_{10}H_{19}O_7P$. Calculated %: P 10.99. Found M 262, 272 (Rast). Calculated: M 282.

SUMMARY

1. The reaction of esters of glycolic acid with phosphorus trichloride, ethoxydichlorophosphine, and dipropoxychlorophosphine has been explored.

2. It has been found that when phosphorus trichloride is reacted with the ethyl ester of glycolic acid, we get an isomer containing pentavalent phosphorus (I), instead of the normal product $P(OCH_2COOC_2H_5)_3$ containing trivalent phosphorus. An explanation is provided for this phenomenon.

3. Dipropyl-(carbopropoxymethyl) phosphite (II) has been synthesized by two methods.

4. It has been established that the dipropyl-(carbopropoxymethyl) phosphite is partially rearranged to a compound with pentavalent phosphorus (III) during the synthesis.

5. The dipropyl-(carbopropoxymethyl) phosphite has been rearranged by the action of a chloroacetate, thus effecting the synthesis of (III). This synthesis has established the structure of the ester, secured as a by-product of the synthesis of dipropylcarbopropoxymethyl phosphite.

6. It has been established that rearrangement of the dipropyl-(carbopropoxymethyl) phosphite yields another product (IV), in addition to the normal product (III). An explanation is advanced for the formation of (IV), and its composition has been established.

7. Seven compounds of a new type, not previously described in the literature, have been synthesized during this research.

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Received July 5, 1950

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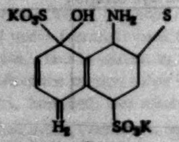
RESEARCHES ON BISULFITE COMPOUNDS

XVI. THE BISULFITE COMPOUND OF 1-AMINO-8-NAPHTHOL-2,4-DISULFONIC ACID

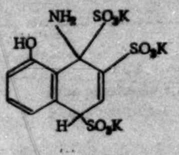
V.N. Ufimtsev and M.I. Chernyak

When 1-amino-8-naphthol-2,4-disulfonic acid is heated with solutions of sodium or potassium bisulfite, the reactions that are typical of this aminoaphthol sulfo acid quickly disappear, and its bisulfite compound is formed. It is impossible to forecast the direction taken by the reaction or the structure of the compound formed, since both the amino and the hydroxy groups attached to the naphthalene nucleus can react with the bisulfite. Moreover, the amino group at the 1 position is exposed to the activating influence of the sulfo group at the 4 position, on the one hand, and to the deactivating influence of the sulfo group at the 2 position on the other [1]. N. N. Vorozhtsov, Sr. [2] states that when 2,4-(bisbenzeneazo)-1-naphthol is heated with sodium bisulfite, which constitutes an analogous case, the bisulfite compound is produced normally.

After the heating of 1-amino-8-naphthol-2,4-disulfonic acid with bisulfites was complete, the resulting solution was found to contain a small amount of the initial product and larger quantities of mineral salts (the sulfite, the bisulfite, and the sulfate), in addition to the expected bisulfite compound. We utilized the method of precipitating the sulfates and sulfites with a barium carbonate solution, described previously [3], to purify the product. Evaporating the resultant filtrates threw down the sodium and potassium salts of the bisulfite compound (it being much easier to recover and purify the potassium salt), which upon analysis proved to contain nitrogen, with one molecule of the bisulfite added to the molecule of 1-amino-8-naphthol-2,4-disulfonic acid. Of the two possible formulas:



(I)



(II)

(I) represents the structure of the synthesized bisulfite compound, since the latter is incapable of coupling with diazonium compounds, whereas it is readily diazotized by treatment with a nitrite in an acid medium, after which it forms dyes by coupling with various azo constituents, i.e., it contains an amino group attached to the aromatic portion of the ring.

EXPERIMENTAL

1. Sodium salt of the bisulfite compound of 1-amino-8-naphthol-2,4-disulfonic acid. 140 grams of the 51% monopotassium salt of 1-amino-8-naphthol-2,4-disulfonic acid (= 71.4 g of the 100% product = 0.2 mole) was refluxed with 25 ml of a 25% sodium hydroxide solution and 200 ml of a sodium bisulfite solution (sp. gr. 1.32) in a round-bottomed flask for 12 hours. The resultant solution was processed by carefully adding a concentrated solution of barium carbonate until the sulfate and sulfite ions were precipitated (no excess!), the precipitated insoluble barium salts being filtered out and washed with a little water. The filtrate was evaporated to 310 ml on a water bath and precipitated with 1120 ml of methanol; this yielded 32.1 g of a yellowish product, which is very readily soluble in water. Double recrystallization from water yielded 4.1 g of the slightly greenish crystalline sodium salt of the bisulfite compound.

0.1508 g, 0.1801 g substance: 0.0610 g, 0.0723 g Na_2SO_4. 0.1904 g substance: 0.0240 g H_2O. Found %: Na 13.10, 13.00; H_2O 12.60. $C_{10}H_8O_{10}S_3NNa_3 \cdot 3\frac{1}{2}H_2O$. Calculated %: Na 13.01; H_2O 11.89.

2. Potassium salt of the bisulfite compound of 1-amino-8-naphthol-2,4-disulfonic acid. 140 grams of the 51% monopotassium salt of 1-amino-8-naphthol-2,4-disulfonic acid was refluxed for 12 hours in a round-bottomed

flask with 15 g of potassium hydroxide and 500 ml of a 20.5% potassium bisulfite solution. The solution was treated with barium carbonate as specified in the synthesis of the sodium salt. When the filtrate was evaporated to 300 ml and then cooled, a finely crystalline precipitate was thrown down; it was filtered out, washed with methanol and ether, and dried, its weight being 30.5 g. The synthesized substance was recrystallized twice from three times its weight of 50% methanol, washed with methanol and ether, and dried in a vacuum desiccator; colorless needles with blunted ends, weight 11.65 g.

0.1470 g, 0.1513 g, 0.1498 g substance; 0.0690 g, 0.0713 g, 0.0710 g K_2SO_4. 3.462 mg, 4.594 mg substance: 2.756 mg, 3.689 mg CO_2; 0.618 mg, 0.949 mg H_2O. 6.824 mg, 6.931 mg substance: 0.146 ml N_2 (21.8°, 736.3 mm), 0.152 ml N_2 (22°, 736.5 mm). Found %: K 21.06, 21.15, 21.27; C 21.72, 21.92; H 2.00, 2.31; N 2.40, 2.46. $C_{10}H_8O_{10}S_3NK_3 \cdot 2H_2O$. Calculated %: K 21.26; C 21.77; H 2.19; N 2.54.

The synthesized bisulfite compound is not coupled in a soda medium with solutions of phenyl- and p-tolyldiazonium chlorides, nor does it give off sulfur dioxide when boiled with dilute sulfuric acid.

When its dilute solutions are heated with caustic alkalies, the bisulfite compound decomposes into a sulfite and the initial 1-amino-8-naphthol-2,4-disulfonic acid, exhibiting the following characteristic reactions: a) evolution of sulfur dioxide when acidulated with dilute sulfuric acid and then boiled; b) production of the brown solution of a diazo compound when acidulated and diazotized; c) coupling with diazoniums in soda, yielding the corresponding azo dyes.

When the bisulfite compound is diazotized, we get diazo compounds that couple readily with azo constituents in a soda medium, yielding dyes whose tones are perceptibly different from those of the analogous dyes produced by diazotizing and coupling the 1-amino-8-naphthol-2,4-disulfonic acid itself.

Azo constituent	Diazo constituent	
	1-Amino-8-naphthol-2,4-disulfonic acid	Its bisulfite compound
	Color of the dye solution	
2-Naphthol-6-sulfonic acid	Yellowish-brown	Yellowish-red
2-Naphthol-3,6-disulfonic acid	" "	Red
1-Amino-8-naphthol-2,4-disulfonic acid	Greenish-brown	Wine-red
1-Amino-8-naphthol-3,6-disulfonic acid	Orange-brown	Violet-red

The dyes prepared from the bisulfite compound of 1-amino-8-naphthol-2,4-disulfonic acid are decomposed when heated briefly with caustic alkalies, splitting off the bisulfite and thus being transformed into dyes that are identical with those synthesized from the 1-amino-8-naphthol-2,4-disulfonic acid itself by diazotizing it and coupling it with the corresponding azo constituents.

SUMMARY

When 1-amino-8-naphthol-2,4-disulfonic acid is treated with potassium or sodium bisulfite, its bisulfite compound is produced. In this reaction only one molecule of the bisulfite reacts with the hydroxy group; the amino group is not affected by the reaction, owing to the deactivating influence of the sulfo group at the 2 position of the naphthalene nucleus.

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September 29, 1950

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Intermediates

THE REACTIONS OF GLYCIDOL AND ITS ETHERS WITH ACID AMIDES

IV. THE REACTIONS OF GLYCIDOL ETHERS WITH FORMAMIDE AND ACETAMIDE

F. G. Ponomarev

As we have shown in one of our previous reports [1], the methyl and ethyl ethers of glycidol react with formamide, yielding the N-mono- and N,N-disubstitution derivatives of formamide: $HCONHCH_2{-}CHOH{-}CH_2OR$ and $HCON(CH_2{-}CHOH{-}CH_2OR)_2$. We later showed [2] that the reaction of these ethers with acetamide likewise involved the formation of two products:

$$CH_3CONH{-}CH_2{-}CHOH{-}CH_2OR \text{ and } CH_3CON(CH_2{-}CHOH{-}CH_2OR)_2,$$

where (as in the first case) R = CH_3 and C_2H_5.

We naturally supposed that this reaction would follow the same course with the higher members of the homologous series of ethers. This was borne out by experiments that form the topic of the present report. Reacting the isopropyl ether of glycidol with the amides of formic and acetic acids and reacting the n-butyl ether with acetamide give rise to mono- and disubstitution derivatives of the amides:

$$HCONH{-}CH_2{-}CHOH{-}CH_2OC_3H_7 \text{ and } HCON(CH_2{-}CHOH{-}CH_2OC_3H_7)_2,$$
$$CH_3CONH{-}CH_2{-}CHOH{-}CH_2OR \text{ and } CH_3CON(CH_2{-}CHOH{-}CH_2OR)_2,$$

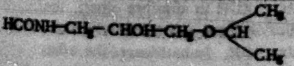
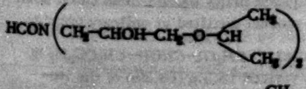
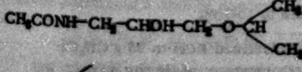
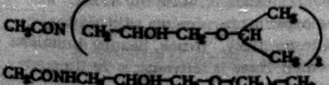
where R = iso-C_3H_7 and n-C_4H_9. The principal product was the monosubstituted amide in every instance. The percentages of the disubstituted amide were lower, which is only natural, as it is formed from the monosubstituted product by the reaction of the latter with new molecules of the ether.

These results justify us in the assumption that the action of glycidol ethers upon acid amides, resulting in the simultaneous formation of two products, is a universal reaction in the glycidol ether series. It is worthy of note that as the molecular weight of the glycidol ethers rises, their ability to react with acid amides diminishes. Of the four ethers investigated under identical conditions, the methyl ether of glycidol reacts most easily with the amides of formic and acetic acid. This is proved by the fact that the aggregate yield of the N-mono- and N,N-disubstituted products exceeds 65% when the methyl ether is reacted with formamide and acetamide, while the product yield of the reaction of the ethyl, isopropyl, and n-butyl ethers of glycidol with these amides is 37-40%, based on the ether.

The isopropyl and n-butyl ethers do not react with formamide or acetamide under ordinary conditions, so that the reaction mixture had to be heated to 150° for 10 hours and sodium hydroxide had to be employed as a catalyst. It is worthy of note that ammonia and amines react rather energetically with these same four glycidol ethers even at room temperature.

The constants of the synthesized substances are given in Table 1.

TABLE 1

Substance	Boiling point (at 4 mm)	d_4^{15}	n_D^{15}	MR_D Calculated	MR_D Experimental
 $HCONH{-}CH_2{-}CHOH{-}CH_2{-}O{-}CH(CH_3)_2$	122-127°	1.0721	1.4570	41.07	40.95
 $HCON\left(CH_2{-}CHOH{-}CH_2{-}O{-}CH(CH_3)_2\right)_2$	202-208	1.0677	1.4620	72.39	71.42
 $CH_3CONH{-}CH_2{-}CHOH{-}CH_2{-}O{-}CH(CH_3)_2$	90-93	1.0428	1.4435	45.69	44.63
 $CH_3CON\left(CH_2{-}CHOH{-}CH_2{-}O{-}CH(CH_3)_2\right)_2$	198-205	1.0215	1.4462	77.01	76.05
$CH_3CONHCH_2{-}CHOH{-}CH_2{-}O{-}(CH_2)_3{-}CH_3$	110-114	1.0151	1.4410	50.31	49.26
$CH_3CON[CH_2{-}CHOH{-}CH_2{-}O{-}(CH_2)_3CH_3]_2$	206-210	1.0011	1.4451	86.31	84.94

All the synthesized substances are colorless or faintly yellowish liquids, mobile (monosubstituted) or slightly mobile (disubstituted), with a peculiar odor. They can be kept in sealed tubes for a long time without change. They are freely soluble in alcohol, ether, and acetone, and sparingly so in water. The monosubstituted amides are more highly thermally stable than the disubstituted ones.

EXPERIMENTAL

The glycidol ethers required for the reaction were prepared from the respective ethers of glycerol α-monochlorohydrins, which in turn were prepared in two ways. The isopropyl ether (chloroisopropylin) and the butyl ether (chlorobutylin) were prepared by heating epichlorohydrin with isopropyl and butyl alcohols, respectively, in the presence of H_2SO_4 by the method described for the synthesis of chloromethylin [3], the respective yields being 26.5 % and 28.8% of the theoretical. The yield is increased 150% when $BF_3 \cdot O(C_2H_5)_2$ is used as a catalyst, i.e., the yield of the isopropyl ether rises to 67%, and that of the n-butyl ether to 74.4%.

1. Reaction of isopropyl and n-butyl alcohol with epichlorohydrin in boron fluoride ethyl etherate. $BF_3 \cdot O(C_2H_5)_2$ was added to a five to eightfold excess of the absolute alcohol, the quantity added constituting 0.05-0.3% of the total of the reagents, after which the epichlorohydrin was added in small portions while the mixture was chilled to −10°. Heat was evolved. Two hours later the reaction mixture was fractionated with a three-bulb dephlegmator, the boron fluoride being decomposed before distillation by the addition of KOH.

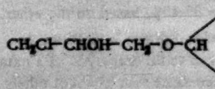
a) 25.0 grams (0.27 mole) of epichlorohydrin and 131 g of absolute isopropyl alcohol, plus 0.8 ml (0.5%) of the catalyst yielded 28.2 g (67% of the theoretical) of the isopropyl ether of glycerol α-monochlorohydrin.

B.p. 180−184°; d_4^{20} 1.0910; n_D^{20} 1.4405; MR_D 36.91; Calculated 37.94. Found %: Cl 22.76. $C_6H_{13}O_2Cl$. Calculated %: Cl 23.20.

b) 36.9 g (0.4 mole) of epichlorohydrin and 150 ml of absolute butyl alcohol, plus 0.1 ml (0.05%) $BF_3 \cdot O(C_2H_5)_2$ yielded 51.5 g (77% of the theoretical) of the n-butyl ether of glycerol α-monochlorohydrin under the foregoing conditions.

B.p. 201−205°; d_4^{20} 1.0660; n_D^{20} 1.4428; MR_D 41.45; Calculated 41.39. Found %: Cl 20.80. $C_7H_{15}O_2Cl$. Calculated %: Cl 21.32.

The constants of these chloroethers are given in the literature as follows [4]:



$CH_2Cl{-}CHOH{-}CH_2{-}O{-}CH(CH_3)_2$ b.p. 87−87.5° at 20 mm; d_4^{20} 1.0530; n_D^{20} 1.4370; MR 37.96.

$CH_2Cl{-}CHOH{-}CH_2{-}O{-}(CH_2)_3{-}CH_3$ b.p. 110−111° at 20 mm; d_4^{20} 1.0444; n_D^{20} 1.4420; MR 42.22.

These ethers are colorless liquids with a specific odor, freely soluble in alcohol and ether, but slightly so in water. They can be kept without change for a long time in stoppered bottles.

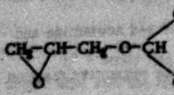
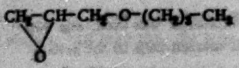
2. Synthesis of the isopropyl and n-butyl ethers of glycidol. The glycidol ethers were synthesized by reacting the glycerol chloroethers we had synthesized with the calculated quantity of KOH in absolute ether: the isopropyl ether by refluxing on a water bath in a flask fitted with a calcium chloride tube, and the butyl ether of glycidol by agitating the mixture without applying any heat and gradually adding KOH. In both cases the ether layer was decanted from the precipitate after the reaction was over, the precipitate being washed three times with absolute ether (15 ml portions), the ether driven off on a water bath, and the product distilled at ordinary pressure.

a) Adding 22 g (0.4 mole) of finely pulverized KOH to 30.5 g (0.2 mole) of $CH_2Cl{-}CHOH{-}CH_2OC_3H_7$ in 40 ml of absolute ether and heating the mixture on a water bath for 1.5 hours yielded 15.5 g (66.8%) of the isopropyl ether of glycidol. Heating for a longer time (4-6 hours) reduced the yield to 10-15%.

b) When the same method was used, adding 16.8 g (0.3 mole) of finely pulverized KOH to 25 g $CH_2Cl{-}CHOH{-}CH_2OC_4H_9$ in 30 ml of absolute ether in the course of one hour at room temperature, while the mixture was vigorously agitated, yielded 12.5 g (64.4%) of the n-butyl ether. When these experiments were run with heating on a water bath for 1.5 or 6 hours, the yields of the ether were 57.2 and 43.1%, respectively. Hence, heating diminishes the reaction product yield, as was the case in the synthesis of the isopropyl ether. There is reference in the literature to the securing of a 66.6% yield of the isopropyl ether of glycidol and 87.5% of the n-butyl ether [4].

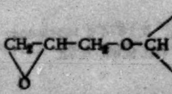
The constants of the synthesized ethers are given in Table 2.

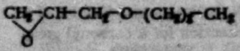
TABLE 2

Formula	Boiling point	d_4^{15}	n_D^{15}	MR_D	
				Calculated	Experimental
	131–134°	0.9285	1.4122	31.24	31.16
	164–166	0.9142	1.4160	35.86	35.73

The ethers are colorless, highly mobile liquids. They distil without vacuum and are freely soluble in alcohol, acetone, and ether, and sparingly in water. The isopropyl ether has a faint fragrance, while the butyl ether has a stronger one.

The following constants are given in the literature for these ethers [4]:


b.p. 68° at 65 mm; d_4^{25} 0.9139; n_D^{25} 1.4068; MR 31.272.


b.p. 69.7° at 20 mm; d_4^{25} 0.9087; n_D^{25} 1.4150; MR 35.873.

3. Reaction of glycidyl isopropyl ether with formamide (together with V. N. Petrova). 3 g of formamide and 9.2 g of the ether (20 % excess) were refluxed together in a flask on an oil bath at 140-150° for 10 hours. When heating was over, the reaction product was fractionated in vacuo twice, yielding 2.4 g (18.8%) of N-propanol-2-isopropoxy-3-formamide and 1.5 g (13.6%) of N,N-di-(propanol-2-isopropoxy-3)-formamide. 3.5 g of a tacky polymer was left in the distilling flask. When analogous conditions were used for this test, but employing a slight pressure (in tightly closed tubes), the disubstituted formamide was the principal product. Attempts to react the isopropyl ether with formamide in a dilute solution of diethyl ether were unsuccessful. Heating 4.8 g of the isopropyl ether for 10 hours with 1.35 g of formamide in ether containing two drops of NaOH did not result in formation of the expected substituted formamides.

The resultant products were colorless liquids that were freely soluble in ether and acetone and sparingly so in water.

Analysis of N-propanol-2-isopropoxy-3-formamide.

0.1290 g substance: 7.85 ml 0.1 N H_2SO_4 (Kjeldahl) Found %: N 8.51. $C_7H_{15}O_3N$. Calculated %: N 8.69.

Analysis of N,N-di-(propanol-2-isopropoxy-3)-formamide.

0.1458 g substance: 5.44 ml 0.1 N H_2SO_4. 0.1314 g substance: 4.76 ml 0.1 N H_2SO_4. 0.1616 g substance: 12 ml 0.1 N NaOH. Found %: N 5.22, 5.07; OH 12.63. $C_{13}H_{25}O_3N(OH)_2$. Calculated %: N 5.05; OH 12.33.

The OH was determined by the method described in our previous paper [1].

The acetate was prepared by reacting the N,N-di(propanol-2-isopropoxy-3)-formamide with acetic anhydride containing a drop of concentrated H_2SO_4.

B.p. 88–91° at 5 mm; d_4^{15} 1.0560; n_D^{15} 1.4459; MR_D 91.60; Calculated 91.25.

0.1756 g substance: 4.33 ml 0.1 N H_2SO_4. 0.1248 g substance: 2.96 ml 0.1 N H_2SO_4. Found %: N 3.45, 3.32. $C_{17}H_{31}O_7N$. Calculated %: N 3.87.

4. Reaction of glycidyl isopropyl ether with acetamide (together with V. T. Kryuchkova). 5.3 g of

acetamide, 12.5 g of the ether (20% excess), and 3 drops of conc. H_2SO_4 were heated together in a sealed glass tube to 150° on an oil bath for 10 hours. The reaction mixture was chilled to −10° to eliminate the unreacted acetamide, and then after part of the amide had been removed, the mixture was processed three times with 15-ml portions of absolute ether; this processing yielded a total of 1.3 g (24%) of the unchanged acetamide. After the ether had been driven off on a water bath, the reaction product was fractionated in vacuo twice. This yielded 4 g (21.2%) of N-propanol-2-isopropoxy-3-acetamide and 3.1 g (19.8%) of N,N-di-(propanol-2-isopropoxy-3)-acetamide. In the flask there remained 0.6 g of a tacky polymer. The same two products were formed in tests run under similar conditions, but without utilizing NaOH as a catalyst, though the yields were lower.

a) 2.3 g of acetamide and 5.4 g of the ether yielded 1.3 g (16%) of the N-monosubstituted acetamide and 0.7 g (10.4%) of the N,N-disubsubstituted acetamide.

b) 5 g of acetamide and 12 g of the ester yielded 2.5 g (13.8%) and 1.5 g (9.9%) of the respective reaction products.

The aggregate yield of reaction products was 23-26% in the tests in which no catalyst was used, and 40% in the tests that employed NaOH as a catalyst. The unchanged acetamide recovered totaled 24% in the tests using a catalyst and 50% in the tests without one.

The resultant products – the N-mono- and the N,N-disubstituted acetamides – were colorless or faintly colored, oily liquids with a specific odor, which were freely soluble in alcohol, ether and acetone, and sparingly so in water.

Analysis of N-propanol-2-isopropoxy-3-acetamide.

0.0928 g substance: 5 ml 0.1 N H_2SO_4. 0.1082 g substance: 5.81 ml 0.1 N H_2SO_4. 0.1674 g substance: 9.33 ml 0.1 N NaOH. 0.0938 g substance: 5.29 ml 0.1 N NaOH. Found %: N 7.60, 7.52; OH 9.47, 9.58. $C_8H_{16}O_2N(OH)$. Calculated %: N 7.99; OH 9.70.

2.5 g of N-propanol-2-isopropoxy-3-acetamide was oxidized with sodium dichromate, yielding 1 g of an oily liquid with a b.p. of 79-84° at 7 mm; n_D^{20} 1.440, which exhibited a positive reaction for a carbonyl group with phenylhydrazine.

Analysis of N,N-di-(propanol-2-isopropoxy-3)-acetamide.

0.1206 g substance: 3.87 ml 0.1 N H_2SO_4. 0.1138 g substance: 3.77 ml 0.1 N H_2SO_4. 0.1554 g substance: 11 ml 0.1 N NaOH. 0.1230 g substance: 8.78 ml 0.1 N NaOH. Found %: N 4.41, 4.63; OH 12.03, 12.13. $C_{14}H_{27}O_3N(OH)_2$. Calculated %: N 4.81; OH 11.68.

5. Reaction of glycidyl n-butyl ether with acetamide (together with L. N. Khopina). Reacting 4 g of acetamide with 10.6 g of the ether (20% excess) and 3 drops of conc. NaOH under the conditions described above yielded 4 g (25.9%) of N-propanol-2-butoxy-3-acetamide and 1.5 g (11.5%) of N,N-di-(propanol-2-butoxy-3)-acetamide. The unchanged acetamide that was recovered totaled 26%. The distilling flask contained a residue of 1.3 g of a tacky polymer.

The synthesized substances were slightly yellowish, oily liquids with a specific odor, freely soluble in alcohol and ether, slightly so in water, and insoluble in benzene.

Analysis of N-propanol-2-butoxy-3-acetamide.

0.1958 g substance: 9.18 ml 0.1 N H_2SO_4. 0.1684 g substance: 8.16 ml 0.1 N H_2SO_4. 0.1312 g substance: 6.2 ml 0.1 N NaOH. 0.1768 g substance: 8.57 ml 0.1 N NaOH. Found %: N 6.56, 6.78; OH 8.03, 8.24. $C_9H_{18}O_2N(OH)_2$ Calculated %: N 7.40; OH 8.98.

2 g of N-propanolbutoxyacetamide was distilled in vacuo over 1 g of $KHSO_4$, yielding 0.8 g of a substance with a b.p. of 100-105° at 8 mm; n_D^{18} 1.430: Brominating this substance in chloroform yielded 0.6 g of a colorless viscous oil, which crystallized in the receiver. The crystals fused at about 36°, exhibited a qualitative reaction for bromine, and contained nitrogen.

0.1016 g substance: 3.26 ml 0.1 N H_2SO_4. Found %: N 4.49. $C_4H_{17}O_2Br_2N$. Calculated %: N 4.23.

These figures indicate that under the conditions described the N-propanolbutoxyacetamide is dehydrated by anhydrous $KHSO_4$ to a product with a double bond, which yields upon bromination a dibromide, the apparent structure of which is : $CH_3-CONH-CHBr-CHBr-CH_2-O-(CH_2)_3-CH_3$. The substance was not analyzed further because of the small quantities available.

Analysis of N,N-di-(propanol-2-butoxy-3)-acetamide.

0.1296 g substance: 3.57 ml 0.1 N H_2SO_4. 0.1554 g substance: 4.39 ml 0.1 N H_2SO_4. 0.2110 g substance: 12.67 ml 0.1 N NaOH. 0.1798 g substance: 10.91 ml 0.1 N NaOH. Found %: N 3.85, 3.95; OH 10.20, 10.31. $C_{16}H_{31}O_3N(OH)_2$. Calculated %: N 4.38; OH 10.65.

The polymer, formed, as indicated, in the reaction of the foregoing ethers with the acid amides, is a tarry substance that is freely soluble in alcohol and ether and sparingly so in water. Upon standing it is converted into a semisolid product that contains 3.2-3.7% of nitrogen.

SUMMARY

1. A study has been made of the reaction of glycidyl isopropyl ether with the amides of formic and acetic acid and the reaction of the n-butyl ether with acetamide.

2. It has been shown that in this reaction N-mono- and N,N-disubstituted amides are formed simultaneously in this reaction, the N-monosubstituted amide being the principal product.

3. The products of these reactions have been isolated and identified: N-propanol-2-isopropoxy-3-formamide, N,N-di-(propanol-2-isopropoxy-3)-formamide, N-propanol-3-isopropoxy-3-acetamide, N,N-di-(propanol-2-isopropoxy-3)-acetamide, N-propanol-2-butoxy-3-acetamide, and N,N-di(propanol-2-butoxy-3)-acetamide.

4. It has been found that the reactivity of the glycidol ethers with formamide and acetamide diminishes as their molecular weight is increased.

5. It has been noted that boron fluoride is a better catalyst than H_2SO_4 in the addition reactions of isopropyl and n-butyl alcohols to epichlorohydrin.

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Received October 10, 1950

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STRUCTURAL CHANGES OF RUBBER CAUSED BY THE ACTION OF MOLECULAR OXYGEN

V. THE DESTRUCTIVE DISSOLUTION OF VULCANIZED SYNTHETIC RUBBERS

Z. Tarasova and B. Dogadkin

We have previously described [1,2] the process involved in the destructive dissolution of vulcanized natural rubber and the properties of the products formed as a result of this process. We showed that the vulcanized rubber does not dissolve when heated to 140° in hydrocarbon media or when acted upon by peptizers and polarizing substances added to the solvent, provided oxygen is rigorously excluded. Only when molecular oxygen is present does heating cause the vulcanized rubber to enter the solvent medium, the process involving the following stages: addition of oxygen → breakdown of the molecular chains at the points where the oxygen has been added → dissolution. When the surface area of the vulcanized rubber remains unchanged, the process continues at a constant rate, depending upon the temperature and the oxygen partial pressure above the solvent. In the general case the variation of the rate of destructive dissolution with the oxygen partial pressure, $\frac{dKa}{d\tau}$, is expressed by the equation:

$$\frac{dKa}{d\tau} = K\frac{\gamma P}{\gamma P + 1},$$

where K and γ are constants.

The broken-down vulcanized rubber has a rather low molecular weight (3600 by the Lamm method), exhibits a Rayleighian scattering of light, and obeys the Einstein viscosimetric equation within a wide range of concentrations. This indicates that massive particles that are envelopes of the vulcanized rubber's space lattice enter solution during destructive dissolution.

The present paper describes the results of experiments that indicate that the phenomenon of destructive dissolution also takes place in synthetic vulcanized rubbers.

1. Effect of the nature of the rubber upon the kinetics of the destructive distillation of vulcanized rubber. Vulcanized sodium-butadiene rubber, butadiene-styrene rubber, chloroprene rubber, and butyl rubber were dissolved.

The vulcanized films were prepared from a benzene cement, applied to the surface of a glass ampoule, using the procedure described previously [1]. The composition of the vulcanized rubbers made of the sodium-butadiene and the butadiene-styrene rubbers was as follows: rubber–100.0; sulfur –2.0; thiuram –0.3; zinc oxide –1.0; and stearic acid –1.0. Optimum vulcanization was obtained in 30 minutes at 143°.

The chloroprene rubber (neoprene) was vulcanized from a mixture of the following composition: rubber – 100.0; magnesium oxide –3.0; rosin –3.0; and zinc oxide –3.0. This mixture was dissolved in dichloroethane. The optimum vulcanization was obtained in 30 minutes at 143°.

The vulcanized butyl rubber had the following composition: rubber –100.0, sulfur –2 0; thiuram –1.0; zinc oxide –2.0; and stearic acid –2.0.

The vulcanized films had mechanical characteristics that were typical for standard rubbers of the foregoing composition. It should be borne in mind that the composition of the vulcanized films prepared from the same paste changes somewhat with time, due to the settling of the insoluble ingredients. That is why comparable tests were made with films that had been produced at the same time.

Heating films of vulcanized sodium–butadiene rubber to 140° in xylene, with oxygen carefully excluded, caused no perceptible dissolution. The vulcanized synthetic rubbers mentioned above, however, dissolved completely when heated in a solvent that was saturated with molecular oxygen.

The procedure used for the experiments on destructive dissolution has been described earlier [1]. The

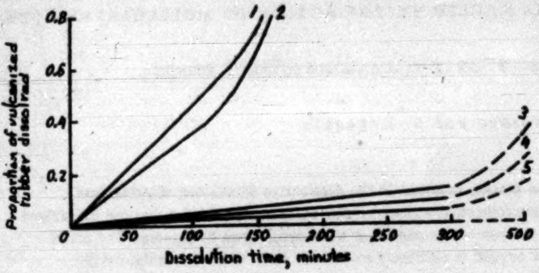

Fig. 1. Kinetic curves of the destructive dissolution of vulcanized rubbers. Temperature 110°, oxygen pressure approx. 760 mm Hg.

1) Natural rubber; 2) chloroprene rubber (neoprene); 3) butadiene–styrene rubber; 4) sodium–butadiene rubber; 5) butyl rubber.

kinetics of the destructive dissolution of vulcanized rubbers (Figure 1) are represented by curves of the same type, which exhibit a straight-line section at the start, corresponding to the period during which the area of the reaction surface remains constant. After this section of the curves the reaction rate rises sharply, owing to an increase in the surface, due to the mechanical destruction of the film and the slippage of its particles into the solution, which results in the uncovering of new parts of the surface. In conformity with the foregoing, the entire process of the destructive dissolution of a finely milled rubber is represented by a straight line. We rejected such procedure, however, since the surface area of a rubber proves to differ even with the most thorough milling.

As we might have expected, the rate of destructive dissolution depends upon the molecular structure of the rubbers (Table 1). The vulcanized rubbers may be arranged in the following order of increasing rate of destructive dissolution: butyl rubber < sodium–butadiene rubber < butadiene–styrene rubber < chloroprene rubber < natural rubber. In the case of rubbers whose molecules do not contain polar groups, this series corresponds to the concentration of double bonds in the principal chains of the polymer. The presence of polar groups retards the process of oxidative destruction. Thus, the vulcanized chloroprene rubber dissolves more slowly than the vulcanized natural rubber, although there are as many double bonds in the molecular chains of both rubbers. The slower dissolution of vulcanized butadiene rubbers may be due to peculiarities in the structure of these rubbers.

TABLE 1

Variation of the Rate of Destructive Dissolution of Vulcanized Rubbers with the Composition and Structure of the Rubber

No.	Rubber	Test temp. (°C)	% of 1,4 structure	Rate of destructive distillation, $\frac{g}{cm^2 \cdot min}$
1	Smoked sheets...........	110°	100	$4.95 \cdot 10^{-5}$
2	Chloroprene (neoprene)	110	100	$3.8 \cdot 10^{-5}$
3	Butadiene–styrene......	110	–	$4.0 \cdot 10^{-6}$
4	Sodium–butadiene.....	110	43	$3.2 \cdot 10^{-6}$
5	Butyl rubber..............	110	100	$3.0 \cdot 10^{-6}$
6	Smoked sheets...........	120	100	$6.75 \cdot 10^{-5}$
7	Butadiene..................	120	59	$2.7 \cdot 10^{-5}$
8	Butadiene..................	120	54	$1.1 \cdot 10^{-5}$
9	Butadiene..................	120	43	$0.62 \cdot 10^{-6}$

The dissolution of vulcanized rubbers when they are heated to temperatures that exclude thermal destruction in a solvent saturated with oxygen is caused by the fact that the reaction of the oxygen with the molecular chains of the spatial structure of the vulcanized rubber is accompanied by a breakdown of the latter at the double bonds, followed by the entrance of the detached particles into the solution. The molecules of natural rubber and of chloroprene rubber are so constructed that the monomer groups are connected into a linear chain at the 1,4 positions. It may be assumed with considerable probability that each act of oxidation and decomposition at the double bonds results in breaking the chain and diminishing the molecular weight. The monomer groups are connected at the 1,4 and 1,2 positions in the molecules of sodium–butadiene and butadiene–styrene rubbers, respectively. The double bonds exist in the main chain as well as in the vinyl side groups there being about 40% of the 1,4-type bonds and about 60% of structures of the 1,2 type in sodium–butadiene rubber.

It is quite obvious that the oxidation and breakdown of the double bonds in the vinyl side groups do not result in the breakdown of the spatial structure that is characteristic of the vulcanizate. Moreover, as Dogadkin has shown [4], the action of oxygen upon the vinyl side groups is responsible for the process of structuralization, inasmuch

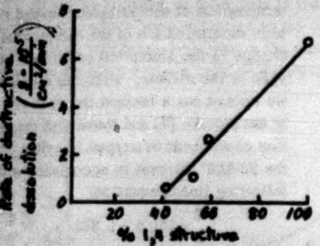

Fig. 2. Variation of the rate of destructive dissolution of vulcanized butadiene rubbers with the percentage of 1,4 structures. Temperature 120°; oxygen pressure approx. 760 mm Hg.

as the oxidation of the side vinyl groups gives rise to polyfunctional molecular chains (without diminishing the initial molecular weight), the oxygen groups of which can interact with one another and with the polymer's double bonds, giving rise to chemical and local intermolecular (hydrogen, orientation) bonds. When we add the possibility of the existence of polymerization processes, brought about by the action of peroxide compounds and—at high temperatures—by the action of heat, we begin to understand why the effectiveness of the destructive action of oxygen is greatly diminished in vulcanized rubbers made of butadiene polymers that contain vinyl side groups. The significance of different positions of the double bonds in the molecular chains of rubber during destructive dissolution is clearly shown in the butadiene polymers that contain varying proportions of the 1,4 and 1,2 structures.

We used rubbers that contained 59, 54, and 43% of the 1,4 structure according to the kinetics of the reaction with perbenzoic acid (the Prilezhayev reaction). The vulcanized rubbers were all prepared from the same recipe using a vulcanized natural rubber in which the percentage of the 1,4 structure was assumed to be 100%. We see in Figure 2 that the rate of destructive dissolution of these vulcanized rubbers is a linear function of the percentage of double bonds in the principal chains (1,4 structures). The fact that the straight line representing the rate of dissolution as a function of the number of 1,4 double bonds does not pass through the origin is evidence that the double bonds in the vinyl side groups with a 1,2 structure present in the polymers give rise to an inverse structuralization process. When the oxygen concentration within the system is held constant, the kinetics of the process may be represented as follows. The rate at which the molecular chains break down, v_1, is proportional to the concentration C of 1,4 double bonds:

$$v_1 = k_1 \cdot C, \tag{1}$$

while v_2, the velocity of the structuralization processes, is proportional to the concentration $C_2 = (1-C)$ of 1,2 double bonds:

$$v_2 = k_2 (1-C). \tag{2}$$

Then V, the overall rate of destructive dissolution, is the algebraic sum of the two process rates:

$$V = v_1 - v_2 = -k_2 + (k_1 + k_2) C. \tag{3}$$

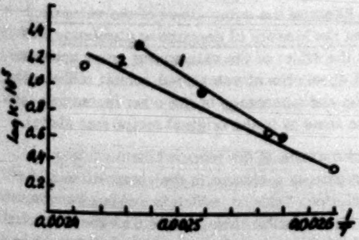

Fig. 3. Variation of the kinetic constants of the destructive dissolution of vulcanized rubbers with temperature: 1) sodium—butadiene rubber; 2) butadiene—styrene rubber.

As we have shown previously [1], the dissolution process takes place at a stationary rate in the surface layer, being governed by the initial concentration of double bonds. Hence, Equation (3) applies to the entire process, provided the surface of the vulcanized rubber being destroyed remains constant. The constants in Equation (3) depend upon the temperature, the oxygen partial pressure, and the absorption coefficient of the oxygen in the solvent. In the case of the dissolution in xylene at 120° and an oxygen pressure of 760 mm of pure vulcanized rubbers that contain tetramethylthiuram disulfide as an accelerator, Equation (3) may be written as follows:

$$V = -4.0 \cdot 10^{-5} + 1.2 \cdot 10^{-6}\, C, \tag{4}$$

where V is given in grams/cm^2·min, and C denotes the percentage of the total number of double bonds in the polymer that is represented by double bonds of 1,4 structure. This equation enables us to determine the percentages of 1,2 and 1,4 structures in the molecules of butadiene polymers experimentally.

TABLE 2

Variation of the Rate of Destructive Dissolution of Vulcanized Natural Rubber with the Composition of the Vulcanizing Group Temperature 109°. Oxygen pressure approx. 760 mm Hg.

Composition of the vulcanizing group, parts by weight	Tensile strength, kg/cm²	% elongation	Permanent elongation, %	Rate of dissolution, $\frac{g \cdot 10^5}{cm^2 \cdot min}$	Combined sulfur, %
Thiuram 0.2 Sulfur 2.0	176	840	6	3.0	1.48
Captax 0.8 Sulfur 2.75	221	850	12	3.87	1.47
Diphenylguanidine 1.0 Sulfur 3.5	190	880	10	2.31	1.35
Cymate 0.3 Sulfur	180	830	8	3.6	–
Vulcacite 0.25 Sulfur 2.0	180	950	8	3.4	–
Santocure 1.0 Sulfur 2.0	314	765	12	4.9	1.48

The polymer's structure likewise affects the apparent activation energy of the process of destructive dissolution. Determination of this variable required the prior determination of the temperature change in the absorption coefficient of oxygen in the solvent. With this objective, we worked out a method together with M. M.Rezinovsky [3] and found that the absorption coefficient of oxygen in xylene rises in the 23-100° interval in accordance with the following linear equation:

$$\frac{1}{A}^{T} = 150.5 + 0.395 \cdot t. \qquad (5)$$

The kinetics of dissolution of the vulcanized rubber are given by the following equation:

$$\frac{dK_{\alpha}}{d\tau} = k[O] \cdot S, \qquad (6)$$

where [O] is the oxygen concentration in the solvent, and S is the surface area of the vulcanized rubber.

If we insert in this equation the values of [O] calculated from Equation (5), the kinetic constants obtained for various temperatures approximately obey the Arrhenius equation (Figure 3). The apparent activation energy of destructive dissolution is 19Cal/mole for a vulcanized natural rubber in the 87-107° range, 31.2Cal/mole for a vulcanized sodium–butadiene rubber in the 116-128° range, and 27.12 Cal/mole for a vulcanized butadiene–styrene rubber in the 114-123° range.

The substantial increase in the activation energy from the natural rubber to the butadiene polymers is due precisely to the presence in the latter of double bonds in the vinyl side groups, which deflect the process into a steric structuralization.

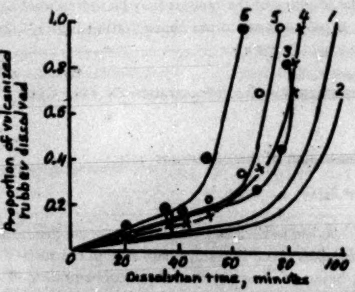

Fig. 4. Kinetic curves of the destructive dissolution of vulcanized natural rubber containing various vulcanization accelerators. Temp. 109°. 1) Captax; 2) Santocure; 3) Cymate; 4) Vulcacite; 5) tetramethylthiuram disulfide; 6) diphenylguanidine.

2. Effect of the composition of the vulcanized rubber upon the kinetics of destructive dissolution. We investigated the effect of the vulcanizing group upon the kinetics of dissolution of vulcanized natural rubber. The composition and percentage of the other ingredients remained the same as in the original recipe (see above).

If the nature of the process kinetics is kept unchanged (Figure 4), a change in the composition of the vulcanizing group results in a change in the rate of destructive dissolution (Table 2), which is unrelated to the mechanical properties of the vulcanized films or the percentage of binding sulfur they contain. In view of the fact that the degree of vulcanization of the tested films was the same, the influence of the composition of the vulcanizing group upon the rate of destructive dissolution may be attributed to the chemical nature of the accelerator.

We have previously demonstrated [1] that mercaptans accelerate the dissolution of vulcanized natural rubber, whereas amines retard this process. It is also known [5] that tetramethylthiuram disulfide retards oxidation. As a matter of fact, rubbers that contain thiuram and diphenylguanidine do dissolve more slowly. Accelerators that possess a mercapto group in their molecule accelerate the dissolution of the rubber. This may be explained in either of two ways: in some instances mercaptans accelerate the addition of oxygen; and they retard the polymerization processes.

It should be borne in mind that in the procedure adopted, films of vulcanized rubber that had been extracted in chloroform were subjected to the dissolution process, which eliminated the accelerators that had not reacted during vulcanization. Hence the accelerator or product of its interaction that affected the rate of destructive dissolution in our tests evidently existed in the vulcanized rubber in a combined state.

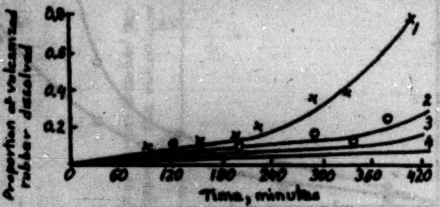

Fig. 5. Kinetic curves of the destructive dissolution of vulcanized sodium-butadiene rubber in various media. Temp. 110°. 1) Xylene; 2) ligroin; 3) toluene; 4) white spirit.

3. Effect of nature of solvent upon kinetics of destructive dissolution of vulcanized sodium-butadiene rubber. Fig. 5 gives the kinetic curves of the destructive dissolution of vulcanized sodium-butadiene rubber in various solvents: xylene, white spirit, cracking gasoline, ligroin, and toluene. The nature of the process kinetics remains unchanged, though the dissolution rate varies. Bearing in mind that the destructive dissolution is brought about by the action of oxygen, we might think that this phenomenon is due to the different solubility of oxygen in the solvents tested.

As has been pointed out, we designed a special device, described elsewhere [3], to determine the solubility of oxygen in organic solvents. In contrast to apparatus of this type previously described, the preliminary degassing of the solvent was effected within the apparatus itself, the degassed solvent being drawn into the adsorption vessel by its own vapor pressure, which makes it possible to fabricate all connections out of glass. As we see in Figure 6, the rate of destructive dissolution of the vulcanized rubbers is a linear function of the solubility of oxygen in the solvents tested. The sole exception to this rule is white spirit. The slowed dissolution of the vulcanized rubber in this solvent is apparently due to the fact that white spirit contains up to 10% of aromatic compounds, which may contain functional groups that retard the reaction with oxygen.

TABLE 3

Variation of the Rate of Destructive Dissolution of Vulcanized Sodium-Butadiene Rubber with the Solubility of Oxygen in the Solvent

Solvent	Temp. at which vulcanized rubber is destructively dissolved, °C	Rate of dissolution of the vulcanized rubber, grams/cm²/min	Temp. at which the oxygen solubility was determined, °C	Oxygen solubility, ml per ml of solvent
Xylene	110	$6.3 \cdot 10^{-6}$	23.5	0.177
Ligroin	110	$4.6 \cdot 10^{-6}$	20	0.156
Toluene	110	$3.05 \cdot 10^{-6}$	20	0.129
White spirit	114	$1.72 \cdot 10^{-6}$	19	0.170

4. Effect of H_2O upon the kinetics of the destructive dissolution of vulcanized sodium-butadiene rubber. The procedure we utilized in studying the influence of water was the same, the sole difference being that oxygen saturated with water vapor was supplied to the device instead of anhydrous oxygen. The presence of water in the oxygen and in the solvent had no effect upon the nature of the kinetics of destructive dissolution of vulcanized natural and sodium-butadiene rubber (Fig. 7), though the rate of dissolution was slowed down in both cases.

We ran experiments to determine the effect of moisture upon the kinetics of oxidation of vulcanized rubbers in a solid film in order to ascertain the mechanism involved in the action of water during destructive dissolution. Oxidation was effected in a Nekrasov adsorption apparatus, the reaction vessels not containing any alkaline absorbents of the volatile oxidation products, of course. Water was introduced into the reaction vessel in the following manner. One or two drops of water were frozen in the vessel, after which the air was pumped out of the vessel, and enough dry oxygen was supplied to allow for the expansion of the volume of oxygen and water as the temperature was raised to the experimental temperature. A parallel oxidation experiment was run with dry oxygen (again without any alkaline absorbents). The films of vulcanized rubber were prepared by applying a rubber paste of the desired composition and vulcanizing by the specified procedure.

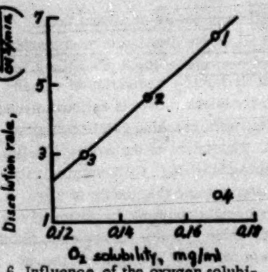

Fig. 6. Influence of the oxygen solubility in various solvents upon the rate of destructive dissolution of vulcanized sodium-butadiene rubber. 1) Xylene; 2) Ligroin; 3) Toluene; 4) White Spirit

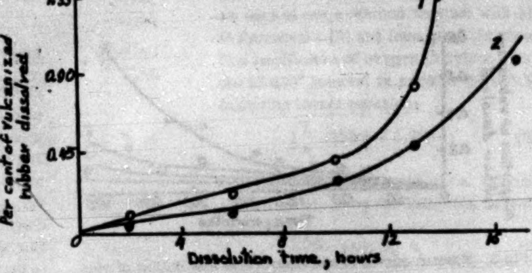

Fig. 7. Effect of water upon the kinetics of the destructive dissolution of vulcanized rubber. Temperature: 105°.
1) Anhydrous oxygen; 2) oxygen containing water vapor with a partial pressure of 22.4 mm Hg.

These experiments indicated that the presence of water in the oxygen, with its partial pressure corresponding to the temperature of the experiment, retards the addition of oxygen, at least during the period of vulcanized rubber oxidation that follows upon the induction period, apparently as the result of the water's decomposing the peroxide. Hence, the retarding action of water upon the dissolution of vulcanized rubber is related to the water's retardation of the addition of oxygen to the rubber (Figure 8).

5. Properties of destructively dissolved vulcanized sodium-butadiene rubber. The destructive dissolution of vulcanized sodium-butadiene rubber produces a faintly yellow opalescent solution. Methanol precipitates some 70% of the substance from solutions whose concentration is no lower than 5%, as a tacky mass that can be completely dissolved in all the ordinary rubber solvents after it is dried in vacuo at room temperature. Chemical analysis of destructively dissolved vulcanized rubber indicates that it contains free carboxyl groups (5.4 mg of carboxylic oxygen per gram of vulcanized rubber), and peroxide groups (1.2% of active oxygen). The total percentage of oxygen in the destructively dissolved vulcanized rubber (after precipitation with methanol) was about 4%).

The partial molecular weight of the destructively dissolved vulcanized rubber was determined by cryoscopy in benzene solutions whose concentration was at least 2%. It ranges from 3600 to 2400, the partial weight exhibiting a tendency to rise as the solution concentration drops. The osmotic partial molecular weight, extrapolated to zero concentration, was 16,000. There is no doubt that this weight represents the high-molecular fraction of the product, because of the permeability of the membrane for the low-molecular fraction.

The viscosity of solutions of the destructively dissolved vulcanized sodium-butadiene rubber (Fig. 9) is a linear function of the equation:

$$\eta_{sp} = 24.0 \cdot v \cdot C, \qquad (7)$$

where $_{sp}$ is the specific viscosity, $\underline{v}$ is the specific volume of the vulcanized rubber, and $\underline{C}$ is the concentration in grams per liter, throughout a wide range of concentrations. The numerical coefficient of this equation makes it possible to calculate the ratio of the axes of the ellipsoid of rotation, corresponding to the dimensions of the particles of the destructively dissolved vulcanized rubber, from Simha's table [6]. This ratio equals 15. According to Pasynsky [7], this ratio is 65 for the molecules of crude sodium-butadiene rubber.

The coefficient in Equation (7) is about 10 times as large as the numerical coefficient in the Einstein equation, which indicates that the effective volume of the particles of the destructively dissolved vulcanized rubber in the solution is 10 times as large as their volume in the solid state. We found that the volume of the initial vulcanized rubber is increased by a ratio of 9.8:1 in xylene. Comparison of these figures indicates that the solution of the destructively dissolved vulcanized rubber contains massive particles that swell up in the solvent, constituting a sort of envelope of the steric structure of the vulcanized rubber.

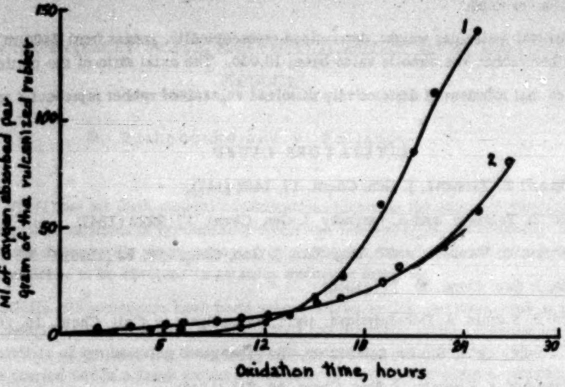

Fig. 8. Effect of moisture upon the kinetics of the absorption of oxygen by vulcanized natural rubber. Temperature: 108°. 1) Dry oxygen; 2) moist oxygen.

Thus the solution of destructively dissolved vulcanized rubber constitutes a new type of lyophilic colloidal system. Some of the characteristics (form, presence of a surface of separation) of the system described class it as a lyophobic colloid, thus differing from the solutions of ordinary high-molecular compounds. The system differs from typical lyophobic colloids in so far as the conditions governing its stabilization are concerned, which is determined by the ability of its particles to swell up in a solvent. What is more, the primary particles of the disperse phase of a solution of a destructively dissolved vulcanized rubber constitute a system of atoms linked by principal valency forces, wherein they differ from the particles in the disperse phase of lyophobic colloids.

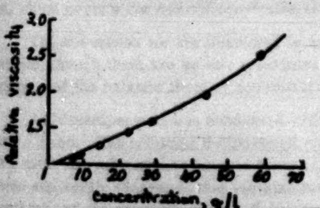

Fig. 9. Variation of the viscosity of solutions of destructively dissolved vulcanized sodium-butadiene rubber with their concentration.

SUMMARY

1. Vulcanized synthetic rubbers dissolve completely when heated in hydrocarbon media that contain molecular oxygen. The kinetics of the destructive dissolution of vulcanized synthetic rubbers are governed by the laws established for the destructive dissolution of vulcanized natural rubber.

2. The rate of destructive dissolution of vulcanized rubbers depends upon the molecular structure of the rubbers. The destructive dissolution rates of vulcanized rubbers increase progressively according to the following series: butyl rubber $<$ sodium-butadiene rubber $<$ butadiene-styrene rubber $<$ chloroprene rubber $<$ natural rubber. The apparent activation energy is 19 Cal/mole for natural rubber, 31.2 Cal/mole for sodium-butadiene rubber, and 27.1 Cal/mole for butadiene-styrene rubber.

3. The rate of destructive dissolution of vulcanized butadiene rubbers is a linear function of the percentage of 1,4 structures in the rubber molecule.

4. The mechanical properties of the vulcanized rubbers have no perceptible effect upon the rate of their destructive dissolution. The type of accelerator employed is of basic importance, their influence corresponding to their effect upon the rate at which oxygen is added.

5. The presence of water retards the dissolution of vulcanized natural and sodium-butadiene rubber, because the H_2O retards the process of oxygen addition.

6. The rate of destructive dissolution of vulcanized rubbers in various solvents is a linear function of the absorption coefficient of oxygen in these solvents.

7. The viscosity of solutions of destructively dissolved vulcanized sodium-butadiene rubber is a linear function of concentration up to 5%.

8. The mean partial molecular weight, determined cryoscopically, ranges from 2400 to 3600 for vulcanized sodium-butadiene rubber, the osmotic value being 16,000. The axial ratio of the particles is 1:15.

9. It is asserted that solutions of destructively dissolved vulcanized rubber represent a special type of colloidal solutions.

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Received October 2, 1950

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NEW TYPES OF TERPENE TRANSFORMATIONS

VIII. SYNTHESIS OF TERPENYLACETOACETIC AND TERPENYLMALONIC ESTERS AND OF THEIR CLEAVAGE PRODUCTS

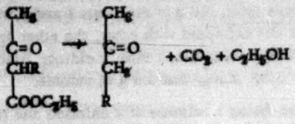
D. Tishchenko and V. Foliadov

In our Report VII [1] we set forth general considerations regarding the anion-exchange reactions of allylic chloroterpenes and described methods of synthesizing ethers and esters of $C_{10}H_{15}OR$ terpenols. We showed that a solvent yielding the same anion as the reagent (say, acetic acid and potassium acetate) must be used if a high yield of the desired product is to be obtained in an anion-exchange reaction.

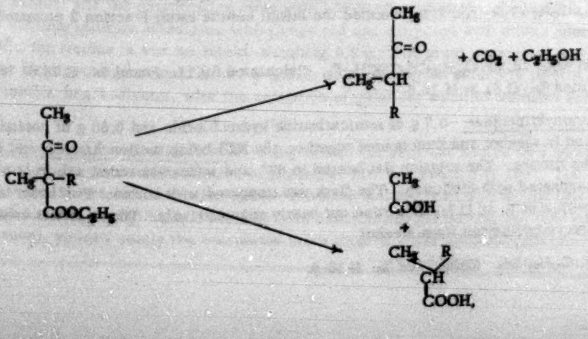
Inasmuch as allylic chloroterpenes have been unknown prior to this, the corresponding acetoacetic and malonic esters have been likewise unknown. We fixed upon the thermally stable 6-chlorodipentene [2] for our research into the feasibility of synthesizing these esters. In accordance with the foregoing, the synthesis of these esters should be carried out in a large excess of malonic or acetoacetic esters as solvents of sodium-substituted esters. But we did not have large quantities at our disposal, so that we synthesized the sodium-substituted esters in toluene at 100°, using calculated quantities of the ester and of sodium and then adding 6-chlorodipentene. It was impossible to utilize absolute alcohol as the solvent, for then the principal reaction product would be 6-ethoxydipentene [1]. The reaction of 6-chlorodipentene with the sodium derivatives of the specified esters in toluene is much slower than with potassium acetate in acetic acid. The reason for this is evidently that toluene is not a good enough ionizing solvent for either the chloroterpene or the sodium-substituted ester, owing to its low dielectric constant, wherein it differs from acetic acid. As a result, the rate of ionization of the chloroterpene, which governs the overall conversion rate, is low, with the consequences that follow therefrom.

The conversion we are interested in are far from finished after 16-24 hours of heating; being only 30-70% complete, though there are no side reactions: the unreacted portion of the chloroterpene being recovered unchanged, and the balance sheet of the initial and synthesized substances tallying.

6-Chlorodipentene was condensed with the sodium derivatives of acetoacetic, methylacetocacetic, and malonic esters. The resulting 6-dipentenyl esters were viscous, high-boiling liquids. The 6-dipentenylacetoacetic ester was subjected to ketonic cleavage, the 6-dipentenylmethylacetoacetic ester being subjected to both ketonic and acidic cleavage, thus yielding hitherto unknown ketones (6-acetonyldipentene and 6-isobutanonyldipentene) and the unknown methyl-6-dipentenylacetic acid.



$$CH_3{-}CO{-}CHR{-}COOC_2H_5 \rightarrow CH_3{-}CO{-}CH_2{-}R + CO_2 + C_2H_5OH$$



$$CH_3{-}CO{-}C(CH_3)(R){-}COOC_2H_5 \rightarrow CH_3{-}CO{-}CH(CH_3){-}R + CO_2 + C_2H_5OH$$

$$CH_3{-}CO{-}C(CH_3)(R){-}COOC_2H_5 \rightarrow CH_3COOH + CH_3(R)CH{-}COOH,$$

where R = 6-dipentenyl.

The dipentenylmalonic ester was saponified to the corresponding dipentenylmalonic acid, from which carbon dioxide was split out to produce dipentenylacetic acid, RCH_2COOH.

The two new ketones are mobile liquids with very pleasant fragrances. Their analyses indicated that they were somewhat impure. Their semicarbazones were secured in an analytically pure state. We were unable to crystallize any of the acids mentioned.

As the cited findings indicate, it is possible to synthesize terpenylacetoacetic and terpenylmalonic esters readily from thermally stable chloroterpenes. This is further [1] confirmation of the feasibility of synthesizing unknown or difficultly accessible terpene derivatives with the same degree of unsaturation and the same carbon skeleton as the original terpene, which we had postulated previously.

EXPERIMENTAL

Synthesis of 6-dipentenylacetoacetic ester. The 6-chlorodipentene had a b.p. of 68° (2 mm); d_4^{20} 0.9926; n_D^{20} 1.4979; the percentage of saponifiable chlorine was found to be 19.5, 19.8; the calculated value being 20.7.

100 ml of anhydrous toluene and 2.7 g of sodium were placed in a round-bottomed flask fitted with a stirrer and a reflux condenser. The flask was heated until the sodium melted, after which the stirrer was stopped and 15.3 g of ethyl acetoacetate was added drop by drop. After 6 hours of stirring at 100° (bath temperature), all the sodium was converted into a gelatinous precipitate of the sodiumacetoacetic ester. The mixture was stirred and heated while 20 g of the chloroterpene was added. Eight hours later, while the precipitate was fully stirred up with the stirrer, a sample was taken with a pipet (the total volume being known) and the NaCl content of the sample was determined. The reaction was 58% complete. Heating and stirring were continued for another 8 hours, after which the reaction was 66.5% complete. The precipitate was suction filtered, washed with toluene, and dissolved in water, the solution being extracted with ether. The percentage of Cl was determined in the aqueous solution; the reaction was 69.6% complete. The coarse method (see above) yielded 66.5%, which indicated that it could be employed to check the progress of the reaction. The ether and the toluene were eliminated from the filtrates, the residue weighing 28.5 g; it was distilled at 0.2 mm, yielding: Fraction 1 (to 55°), 3.85 g; and Fraction 2 (55°), 2.95 g. Fraction 1 colored ferric chloride crimson and contained 9.2% chlorine, i.e., it was a mixture of approximately equal parts of the acetoacetic ester and the chlorodipentene; Fraction 2 contained 20.6% of chlorine (chlorodipentene). The residue was fractionated molecularly at 0.001 mm, yielding: Fraction 1 (bath temperature up to 80°), 1.70 g; Fraction 2 (bath temperature 80-85°), 15.55 g; and a residue of 2.65 g, which did not distil on a boiling water bath.

Fraction 1 contained 12.8% of chlorine and colored $FeCl_3$ crimson, i.e., it contained a chloride and the sought-for ketone ester; Fraction 2 colored $FeCl_3$ red and had the following constants:

d_4^{20} 1.0144; n_D^{20} 1.4891; MR_D 75.18; calculated for the keto form 74.62.
Found %: OC_2H_5 17.8, 17.5. $C_{16}H_{24}O_3$. Calculated %: OC_2H_5 17.1.

Ketonic cleavage of the ketone ester. 16 g of Fractions 1 and 2 was steam-distilled with 140 ml of 7% potassium hydroxide. The distillate was extracted with ether, the ether driven off from the extract, and the residue (10.8 g) fractionated into a small column at 1 mm, yielding: Fraction 1 (53-85°), 1.10 g; Fraction 2 (85-87°), 6.8 g; Fraction 3 (87)–120–122° 2.2 g; and 0.5 g of residue.

Fraction 1 contained chlorine, being a mixture of a chloride and the ketone; the constants of Fraction 3 were d_4^{20} 1.014; n_D^{20} 1.4924; % OC_2H_5 17.4; and it represented the initial ketone ester; Fraction 2 possessed a highly fragrant, slightly sharp odor.

d_4^{20} 0.9353; n_D^{20} 1.4880; MR_D 59.19; $C_{10}H_{15}CH_2COCH_3 \cdot F_2$. Calculated 59.11. Found %: C 78.6, 78.7; H 11.1, 11.2. $C_{13}H_{20}O$. Calculated %: C 81.2; H 10.6.

Semicarbazone of 6-acetonyldipentene. 0.7 g of semicarbazide hydrochloride and 0.65 g of potassium acetate were separately dissolved in alcohol and then poured together, the KCl being suction filtered, and 1.2 g of the ketone being added to the filtrate. The solution was heated to 60°, and water was added a drop at a time until the resulting turbidity disappeared with difficulty. The flask was stoppered with cotton. Two hours later crystals of the semicarbazone with a m.p. of 117-118° settled out nearly quantitatively. The m.p. was constant at 129.5–130° after the fourth recrystallization from alcohol.

Found %: N 16.5, 17.2. $C_{14}H_{23}ON_3$. Calculated %: N 16.9.

Synthesis of 6-dipentenylmethylacetoacetic ester. This was effected under the conditions set forth above. 6.5 g of sodium; 250 ml of toluene; 44 g of methylacetoacetic ester; and 48.5 g of 6-chlorodipentene; 18 hours of heating on a water bath. The reaction product was diluted with an equal volume of water and neutralized, while stirred, with normal nitric acid; the toluene and aqueous layers were separated; and the percentage of Cl in the latter layer was determined. The reaction was 63.4% complete. The toluene was driven off from the toluene layer in a water-jet vacuum with an adapter, the residue weighing 70 g. Molecular fractionation of the residue at 0.001 mm and a bath temperature not in excess of 100° yielded 52.8 g of distillate, the residue totaling 9 g, and the losses 8.2 g, as indicated by the toluene balance sheet. The distillate contained 6.85 g of chlorine, equivalent to 17.4 g of the chloride. If the reaction had been 63.4% complete, we should have gotten 17.8 g of the chloride. 52.35 g of the distillate was fractionated at 1 mm into a column with an efficiency of 3-4 theoretical trays and a reflux ratio of 8-10. Fraction 1 (43-120°) weighed 13.65 g; Fraction 2 (120-135°), 5.05 g; Fraction 3 (135-137°), 30.75 g; the residue was 2.05 g; and the losses 0.85 g. Fraction 3 contained no chlorine.

d_4^{20} 1.017; n_D^{20} 1.4889; MR_D 78.83. $CH_3COC(C_{10}H_{15})(CH_3)COOC_2H_5 \cdot F_2$. Calculated 78.81. Found %: OC_2H_5 16.5. $C_{17}H_{28}O_3$. Calculated %: OC_2H_5 16.2.

Ketonic cleavage of the ester. 19.75 g of the ester and 200 ml of 7% potassium hydroxide were distilled with steam. The oil was extracted from the distillate with ether, the ether being driven off and leaving a residue of 17.4 g. The residue was fractionated at 1.6 mm into a small column with a reflux ratio of 8-10: Fraction 1 (85-102°), 0.5 g; Fraction 2 (102-109°), 3.15 g; Fraction 3 (109-130°), 3.55 g; Fraction 4 (130-138°), 7.15 g; and a residue of 1.05 g. Fraction 4 was the initial ketone ester (d_4^{20} 1.026; n_D^{20} 1.4901). Fractions 2 and 3 were refractionated at 1.25 mm: Fraction 1 (96-98°), 5.2 g; Fraction 2 (98-108°), 0.9 g; and a residue of 0.5 g. The constants of Fraction 1 were: d_4^{20} 0.9378; n_D^{20} 1.4834; MR_D 62.83. $CH_3COCH(CH_3)C_{10}H_{15} \cdot F_2$. Calculated 63.37. The ketone is a liquid with a pleasant fragrance that is somewhat different from that of the preceding one. Its negative exaltation is evidence of its incomplete purity.

Semicarbazone of isobutanonyl-6-dipentene. This was prepared by the method described above. The crystals settled out 24 hours later, rather than after 2 hours, which conforms with the greater degree of branching of this ketone. A constant m.p. of 127-127.5° was attained after three recrystallizations from methanol. Found %: N 16.2, 16.3. $C_{15}H_{27}ON_3$. Calculated %: N 16.0.

Synthesis of the 6-dipentenylmalonic ester. 300 ml of toluene and 2.7 g of sodium. The mixture was heated to 100° and stirred while 29 g of malonic ester was added in the course of 2.5 hours, followed by 20.5 g of the chlorodipentene. Heating lasted 2.5 hours. After cooling, the reaction product was neutralized with dilute nitric acid (1:5). The toluene layer was removed, and the percentage of chlorine in the aqueous layer determined, indicating that the reaction was 35.6% complete. The toluene was driven off from the toluene layer at 12 mm into a column, the residue weighing 44 g. The 52-60° overhead fraction (24.5 g, containing 7.7% of chlorine) was distilled at 0.1 mm, the residue weighing 16.2 g; of the latter 14.3 g was fractionated at 0.01 mm, yielding: Fraction 1 (53-112°), 1.1 g; Fraction 2 (112-113°), 8.7 g; and Fraction 3 (113-119°), 2.5 g.

Fraction 2: d_4^{20} 1.031; n_D^{20} 1.4755; MR_D 80.82. $C_{10}H_{15}CH(COOC_2H_5)_2$. Calculated 80.87.
Found %: OC_2H_5 29.5, 29.1. $C_{17}H_{26}O_4$. Calculated %: OC_2H_5 30.6.

Fraction 3: d_4^{20} 1.025; n_D^{20} 1.4769; MR_D 81.7. % OC_2H_5 29.9. The distillation residue (1.1 g) contains 26.9% of OC_2H_5. The yield of the dipentenylmalonic ester is equivalent to mineralized chlorine.

Saponifying the ester. 7.45 grams of the ester was heated to 100° for 3 hours with 4 g of KOH and 3 ml of water. The alcohol and the unsaponified ester were blown off with steam, the residue being extracted with ether, and the alkaline solution acidulated with Congo red and extracted with ether. The ether was driven off from the extract, the residue, a viscous liquid, weighing 5.9 g. The gram equivalent was found to be 133, the computed value for dipentenylmalonic acid being 119; an acid ester is evidently present as an impurity. The ester is freely soluble in all solvents, with the exception of gasoline; when its solutions are evaporated, a thick oil settles out.

Decomposing dipentenylmalonic acid. 4.9 grams of the acid was heated on a metallic bath until no more carbon dioxide was given off, evolution beginning at 110° and ceasing at 190°. The residue weighed 3.70 g, though it should weigh 3.55 g. The gram equivalent was found to be 228, the calculated value for dipentenylacetic acid ($C_{12}H_{18}O_2$) being 194. The acid contains neutral impurities. The silver salt, prepared in the usual manner, yielded nearly the calculated percentage of silver upon analysis (35.5, 35.6%; calculated 35.7%).

Synthesis of methyl-6-dipentenylacetic acid. 6.7 grams of methyldipentenylacetoacetic ester (see above) was heated to 100° with 17 g of an 82% solution of KOH for 3 hours 45 minutes. Steam was blown through the solution to remove the neutral substances, the solution being extracted with ether after cooling for the same purpose, and then acidulated with Congo red. The oil was extracted with ether, and the ether driven off, the residue weighing 3.6 g. The gram equivalent was found to be 216, the calculated value being 208. The acid was purified by molecular distillation at 0.001 mm and a bath temperature of 80-90°, which reduced the gram equivalent to 210. The acid did not crystallize.

Found %: C 74.4; H 9.9. $C_{13}H_{20}O_2$. Calculated %: C 74.9; H 9.7.

The silver salt was prepared in the usual manner.

Found %: C 49.4; H 6.2; Ag 34.1. $C_{13}H_{19}O_2Ag$. Calculated %: C 49.5; H 6.1; Ag 34.2.

SUMMARY

1. 6-Chlorodipentene has been used to show that terpenylacetoacetic and terpenylmalonic esters can be synthesized.

2. Ketones and acids of the homoterpene series can be prepared from these esters in the usual manner.

3. These facts support our previous postulate that diversified new syntheses can be carried out using the chloroterpenes, yielding hitherto unknown or difficultly accessible derivatives of terpenes in which neither the carbon skeleton nor the degree of unsaturation of the terpene is changed.

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Received September 13, 1950.

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THE FORMATION OF PHENOLS IN THE CATALYTIC CONDENSATION OF ACETONE WITH ACETIC ANHYDRIDE. III

B. N. Dolgov, T. V. Nizovkina, and L. V. Mozzhukhina

When ethyl alcohol is condensed with acetone over an $Al_2O_3-Fe_2O_3$ catalyst at 400-410°, condensate is formed that contains 5% of phenols, the bulk of which consists of 3,5-dimethylphenol [1]. On the basis of the existing research papers and analytic findings the suggestion was put forward that this is a complex process, the first stage of which is the dehydrogenation of ethyl alcohol to acetaldehyde, which then condenses with the acetone, forming the final phenol. In our study of the behavior of several alcohol-ketone systems we secured the corresponding phenols that were predicted by the proposed mechanism; to a certain degree this constitutes a proof that the latter is correct. We also undertook the present research on the acetaldehyde–acetone system to prove that the formation of phenols from alcohols and ketones involves a preliminary stage in which the alcohols are dehydrogenated to aldehydes.

The $Al_2O_3-Fe_2O_3$ catalyst was prepared as described in our preceding report [2], its activity being tested by producing phenols from a mixture of ethyl alcohol and acetone. The phenol yield was 6%. A mixture of acetaldehyde and acetone was passed over this catalyst under varying conditions and the percentage of phenols in the condensate was determined. As in our previous researches, the optimum temperature was found to be 400-410°, as indicated by the following figures:

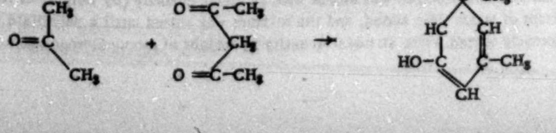
Temperature	380-390°	390-400°	400-410°	410-420°
Per cent of phenols	4.45	5.42	9.4	7.47

The optimum volumetric rate was found to be 31-33. The activity of the catalyst dropped appreciably after 2 hours of operation, but was restored in full after oxygen had been blown through at 450-500°. The deactivation of the catalyst is caused by the deposition of tarry films on the contact surface. The gain in weight totaled 2.56% of the catalyst's weight after 2 hours of operation, or 9.5% of the mixture throughout. The mixture of acetaldehyde and acetone yields nearly twice as much of the phenols as the mixture of ethyl alcohol and acetone (9.5 and 5.1%, respectively).

The condensates constituted a two-layer liquid, consisting of an oily and an aqueous layer. The phenols were extracted by processing the condensate twice with 10% NaOH, after which the alkaline solution was separated from the oil and acidulated with 10% H_2SO_4. Analyses of the condensates indicated that their mean composition is as follows: 9.5% phenols, 33.2% neutral oil, 39.4% unreacted mixture, and 15.3% water. The phenols are probably formed only via the joint condensation of acetaldehyde and acetone, inasmuch as neither the aldehyde nor the acetone by itself yields phenols, as has been proved by special tests. The highest phenol yield is attained with an equimolecular mixture of the reagents (1:1).

Analysis of the phenolic oil indicated that its principal constituent was 3,5-dimethylphenol. We also found a slight percentage of ethylphenol. The production of the former bears out our hypothesis that the condensation involves the intermediate formation of β-diketones as follows:

$$CH_3COCH_3 + HOC-CH_3 \rightarrow CH_3COCH_2CHOHCH_3$$
$$CH_3COCH_2CHOHCH_3 \rightarrow CH_3COCH_2COCH_3 + 2H$$



3,5-Dimethylphenol

The higher fractions of the phenolic oil constituted complex mixtures of high-molecular phenols; we were unable to separate them or to identify the individual phenols by existing methods.

The neutral part of the oil, which was insoluble in alkali, distilled continuously in the 50-250° range. The residue was a black resin (30% of the oil). The composition of the resin was determined by destructive distillation [3]. Analysis of the decomposition products indicated that the resin contains condensed phenols and aldehyde, i.e., its composition is close to that of Bakelite. Treating the phenols obtained by destructively distilling the resin with chloroacetic acid in the presence of NaOH yielded a mixture of aryl glycolic acids with a broad melting point (in the neighborhood of 11°). These results indicate that the condensation of aldehyde with acetone goes much deeper than we had supposed. The formation of individual phenols from the acetaldehyde and the acetone is paralleled by a more thoroughgoing condensation of the aldehyde with the synthesized phenols, yielding phenolic-aldehydic resins. Thus, the phenolic oil consists of only that part of the total phenols secured from the aldehyde and the acetone which did not enter into further condensation. A very rough calculation indicates that 25-30% of phenols are produced per single pass.

The fraction with a b.p. of 50-250° was fractionated into a Todd column, yielding a series of fractions, the investigation of these fractions and the isolation of individual products from them being greatly hampered by the fact that secondary dehydration and polymerization reactions in the flask accompanied the fractionations. We found that all the fractions contained ketones, though only methyl ethyl ketone could be isolated and identified. Unreacted acetaldehyde and acetone were recovered from the neutral aqueous layer.

EXPERIMENTAL

The experiments on the condensation of acetaldehyde with acetone were performed in the usual catalytic apparatus, using a tubular electric furnace (24 cm platform). The temperature was measured with an iron-constantan thermocouple placed in the catalyst zone. The Al_2O_3–Fe_2O_3 catalyst was prepared by introducing the calculated quantity of Al_2O_3, with stirring, into ferric nitrate that had been fused in its own water of crystallization. The resultant mixture was stirred to a thick paste with a 5% solution of starch and dried for half an hour at 70-80°, after which it was formed into coils (2 mm), which were dried out at 100°. After the catalyst had been placed in the reaction tube it was exposed to a strong current of air at 450-500° until no more nitrogen oxides were evolved. In every run, a mixture of acetaldehyde and acetone was passed over 100 ml of catalyst at a volumetric rate of 31-33. The optimum reaction temperature was 400-410°. Ninety runs were made to accumulate a large enough amount of the condensate.

The resulting two-layer condensate was first distilled to drive off the fraction up to 60°, which contained most of the unreacted aldehyde and acetone, after which the contents of the reaction flask separated into two layers: the upper one a dark oil and the lower one a light-yellow aqueous layer with a slightly acid reaction. The aqueous layer distilled at 100°, leaving practically no residue. It was nearly pure water. The oily layer contained no acids. Its phenols were extracted by agitating it twice with 10% NaOH. The phenolate solution was washed with ether to free it of the partially extracted drops of neutral oil and then decomposed with 10% H_2SO_4. The resulting phenols were extracted with ether, dried, and weighed after the ether had been driven off. The neutral part of the oil was given the same treatment after the phenols had been eliminated. A flow-sheet test, with analysis of the condensate, yielded the following results:

Mixture throughput	12.5 g
Condensate secured	11.0 g
Volume of gas evolved	660 ml
Weight of carbon on the catalyst	1.2 g
Weight of aldehyde in trap	0.01 g

Analysis of the phenolic oil. The phenolic oil was fractionated, yielding the following narrow fractions: 1) 177-192°, 0.2 g; 2) 192-196°, 1.3 g; 3) 198-202°, 1.5 g; 4) 203-210°, 2.8 g; 5) 211-214°, 2.8 g; 6) 215-220°, 2.9 g; and 7) 221-226°, 2.1 g. The residue, with a b.p. about 226° (27%) constituted a complex mixture of higher phenols and was not analyzed further. All the fractions were analyzed by the Holzmann and Pilat method of preparing aryl glycol acids [4] to determine the percentages of the individual phenols they contained; part of the tested phenolic fraction was mixed with an equal quantity (by weight) of NaOH, ground to fine powder, a few drops of water were added, and the mixture was stirred until a phenolate was formed, after which it was vigorously stirred while an equal quantity by weight of monochloroacetic acid was added. The reaction was carried out in the cold, giving rise to foaming and the liberation of heat. The resultant melt was dissolved in hot water, the aryl glycolic acids being extracted by adding HCl and extracting with ether. The ether extract was treated with a soda solution to eliminate the unreacted phenol. Acidulating the soda extract precipitated an aryl glycolic acid, which was recrystallized from water. In this manner Fraction 2, with a b.p. of 192-196°, yielded an aryl glycolic acid with an m.p. of 80.5-81.5°, which was 3,5-dimethylphenoxyacetic acid (m.p. of 81°, according to the literature). The same acid was secured from the 198-202° and 211-214° fractions. The mixed melting points of these acids with one another exhibited no depression, which was evidence of their identity. The molecular weight was determined by titration with alkali.

Found %: C 66.34, 66.53; H 6.83, 6.92; M 179, 179.4. $C_{10}H_{12}O_3$. Calculated %: C 66.66; H 6.7; M 180.

The 215-230° fraction yielded an aryl glycolic acid with a broad melting point, which constituted a mixture of two acids, which were separated by fractional crystallization from water. One of them was 3,5-dimethylphenoxyacetic acid (m.p. 79-80.5) while the other was *p*-ethylphenoxyacetic acid (m.p. 96-97°; the m.p. given in the literature is 96-97°). The molecular weight of the latter was determined as 177 (the calculated value being 179). The 203-210° and 221-226° fractions yielded a complex mixture of aryl glycolic acids, from which we were unable to isolate individual acids. Analogous results were obtained when twice and three times the quantities of alkali and monochloroacetic acids were employed.

The neutral part of the oil, separated from the phenols, was driven off at 50-250°, leaving a tacky black resin that solidified upon cooling (30% of the initial oil) within the distilling flask. The distillation product was carefully fractionated into a Todd flask, yielding 13 fractions, which were analyzed individually. All the fractions contained ketones, the fractions that boiled above 90° constituting complicated mixtures, from which no individual component could be isolated. The lower fractions contained 89-96% of unreacted acetone. The latter was determined as a *p*-nitrophenylhydrazone with an m.p. of 146-147°. The 78-82° fraction was found to contain methyl ethyl ketone, as was proved by securing the *p*-nitrophenylhydrazone with an m.p. of 126-127°. The latter exhibited no depression of the melting point when mixed with the *p*-nitrophenylhydrazone secured from known methyl ethyl ketone. The semicarbazone of methyl ethyl ketone, which had an m.p. of 134-136° (the literature gives 136°), was secured and tested in a similar manner.

Found %: N 32.88, 32.74; $C_5H_{11}N_3O$. Calculated %: N 32.53.

The resin left within the flask after the neutral oil had been driven off up to 250° was subjected to dry distillation, the resulting liquid products being analyzed qualitatively. They exhibited a positive silver mirror reaction (acetaldehyde). The phenolic constituents were determined by producing a mixture of aryl glycolic acids, which we were unable to separate into the individual components.

SUMMARY

1. Condensing acetaldehyde with acetone over an $Al_2O_3-Fe_2O_3$ catalyst at 400-410° yields a condensate that contains 9.5% of phenols, of which 3,5-dimethylphenol and ethylphenol were identified.

2. The neutral oil left behind after the phenols had been isolated consists of acetone, methyl ethyl ketone, and a complex mixture of higher ketones.

3. After the neutral oil has been driven off up to 250°, there is left behind in a flask 30% of a black resin of the Bakelite type, containing aldehyde and phenols. A preliminary estimate is that 25-30% of phenols are produced per single pass from acetaldehyde and acetone.

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Received July 24, 1950.

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* See Consultants Bureau translation, p. 691.

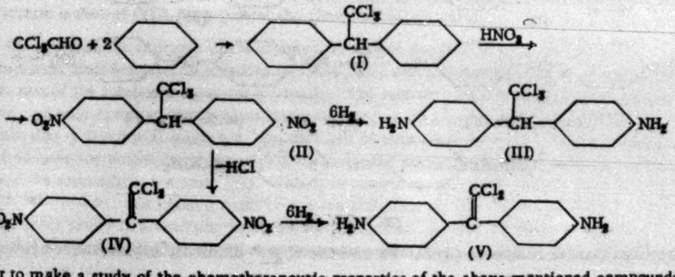
** See Consultants Bureau translation, p. 697.

SYNTHESIS OF 1,1,1-TRICHLORO-p,p'-DIAMINODIPHENYLETHANE AND ITS DERIVATIVES

I. Kh. Feldman and A. I. Zitser

In 1944 the hypothesis was put forward in the literature [1] that the amino analog of the well-known insecticide dichlorodiphenyltrichloroethane (DDT)—1,1,1-trichloro-p,p'-diaminodiphenylethane (III)—might be active against tuberculosis bacilli. Attempts were then made to synthesize this compound, but, to judge from the published findings, only Kirkwood and Phillips [2] succeeded in isolating the diamine (III) in the individual state. The same authors state that the diamine (III) synthesized by them and its unsaturated compound 1,1-dichloro-p,p'-diaminodiphenylethylene (V) retard the growth of tuberculosis bacilli in vitro in a 1:100,000 dilution. They also reported that the compound (III) exhibited a perceptible effect upon experimental tuberculosis in guinea pigs.

We repeated the synthesis of these compounds as follows:



in order to make a study of the chemotherapeutic properties of the above-mentioned compounds.

Condensing chloral with benzene, as indicated by Baeyer [3], results in a nearly quantitative yield of 1,1,1-trichloro-2,2-diphenylethane [1], whose m.p. was 62-64° after crystallization from alcohol. When we repeated the nitration reaction under exactly the same conditions as those described by Kirkwood and Phillips, viz. nitrating with nitric acid (d = 1.5) at 30° and stirring for 4 hours at room temperature, we did not secure a 63% yield of the recrystallized product with an m.p. of 166-167°, as stated by the authors. We obtained only a 25-26% yield of the nitro compound (II) with the stated melting point after two or three recrystallizations from glacial acetic acid. Nor did the carrying out of the reaction as specified by Haskelberg and Lavie [4], who performed nitration at -30°, increase the yield of the pure product.

We have worked out a nitration method that furnishes a 40-43% yield of the pure recrystallized nitro compound with a m.p. of 166-167°. Nitration is carried out in chloroform by a mixture of nitric acid (d = 1.5) or sulfuric acid (d = 1.84) and solid potassium nitrate.

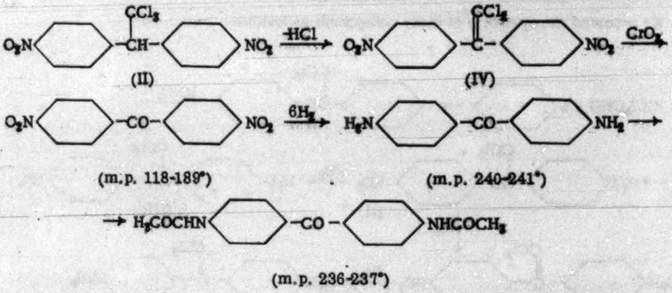
Reducing the nitro compound (II) with Raney's nickel in glacial acetic acid at a pressure of 4 atmospheres yields an amino compound, the m.p. of which was 149-150° after purification. The substance is darkened when it is recrystallized from alcohol, its melting point dropping. The yield of the recrystallized product is very low. We secured a pure product, with a fully satisfactory analysis, by double reprecipitation of the amine from its hydrochloride. The amine thus purified has been kept for several months in a closed container without suffering any change in its melting point or its chlorine content. It is worthy of note that reduction was slow when it was carried out in acetic acid that contained a slight trace of acetic anhydride, and that, instead of the amine (III) we obtained nothing but its acetyl derivative—1,1,1-trichloro-bis-(p-acetylaminophenyl)-ethane, with an m.p. of 258-259°, which was identical with the compound produced by acetylating the amine (III) with acetic anhydride in pyridine.

Eliminating the HCl from the nitro compound (II) by the use of alcoholic alkali results in the synthesis of 1,1-dichloro-bis-(p-nitrophenyl)-ethylene (IV), with an m.p. of 172-173°.

The reduction of (IV) to an amine is effected quite smoothly by using Raney's nickel in glacial acetic acid at normal pressure. The melting point of the amine is 144-145°. Here, too, when we use acetic acid that contains some acetic anhydride, we get nothing but 1,1-dichloro-bis-(p-acetylaminophenyl)-ethylene, with an m.p. of 294-296°, identical with that obtained when we acetylated the unsaturated amine.

We also reduced the nitro compounds (II) and (IV) with stannous chloride and hydrochloric acid. The yield of the amine (III), with an m.p. of 149-150°, rose to 90% of the theoretical under these conditions. The amines synthesized by catalytic reduction and by reduction with stannous chloride were completely identical. When we reduced the nitro compound (IV) by this method, we secured the amine (V) with an m.p. of 144-145°, its yield being 90% of the theoretical, which was identical with the product obtained catalytically.

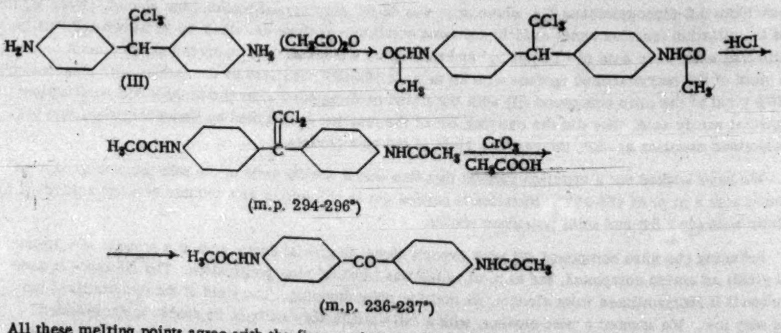
Tests of the action of Compounds (III) and (V) against tuberculosis bacilli, made in the Division of Chemotherapy of our institute by O.A. Makeeva, did not confirm the findings of Kirkwood and Phillips, however. These substances produced only negligible retardation of the growth of tuberculosis bacilli in vitro. This circumstance forced us to repeat the proof of the structure of the compounds we had synthesized as follows:



CCl$_3$
O$_2$N
CH
NO$_2$
-HCl
(II)
CCl$_2$
O$_2$N
C
NO$_2$
CrO$_3$
(IV)
O$_2$N
CO
NO$_2$
6H$_2$
H$_2$N
CO
NH$_2$
(m.p. 118-189°)
(m.p. 240-241°)
H$_3$COCHN
CO
NHCOCH$_3$
(m.p. 236-237°)

It was thus established that the compound (II) has the structure of p,p'-dinitrodiphenyldichloroethylene.

To prove that no rearrangements such as are known in this series take place during reduction, we performed the following series of transformations:



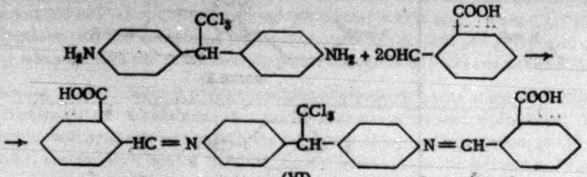
CCl$_3$
H$_2$N
CH
NH$_2$
(CH$_3$CO)$_2$O
(III)
CCl$_3$
OCHN
CH$_3$
CH
NHCO
CH$_3$
-HCl
CCl$_2$
H$_3$COCHN
C
NHCOCH$_3$
CrO$_3$
CH$_3$COOH
(m.p. 294-296°)
H$_3$COCHN
CO
NHCOCH$_3$
(m.p. 236-237°)

All these melting points agree with the figures given in the literature.

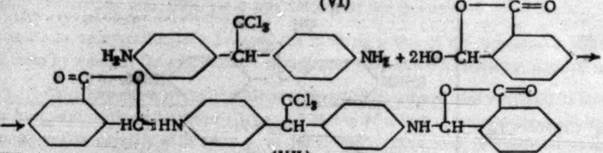
It may therefore be taken as proven that the compound (III) we have synthesized is 1,1,1-trichloro-2,2-bis-(p-aminophenyl)-ethane.

We then obtained the products of the condensation of the amines (III) and (V) with aldehydes. In these condensations we used salicylaldehyde, cotarnine, phthalaldehydic acid, and opianic acid.

Ortho aldehydic acids can react with amines in the aldehydic form or in the tautomeric phthalidic form. Depending upon the form in which these acids react with the amines, the compounds synthesized by us will have either the azomethine structure (VI) or the phthalide structure (VII):



(VI)



(VII)

If the synthesized substances have the structure (VI), they contain an open carboxyl group, whereas if their structure is that of (VII), they possess the closed phthalide group.

To ascertain the structure of the compounds we had synthesized from phthalaldehydic and opianic acids, we investigated their behavior in solutions of alkali, soda and bicarbonate. When the soda solution is allowed to stand, part of the substance dissolves gradually. The substance recovered from the alkali or soda solution (by neutralization with acetic acid) dissolves immediately in a 5% bicarbonate solution and has a different melting point from that of the initial substance. On the basis of these properties, we believe that the compounds we have synthesized have the phthalide structure (VII), whereas the substances isolated from the alkali and soda solutions have the azomethine structure (VI). This is in complete agreement with the assertion of M. M. Shemyakin [5], that phthalaldehydic and opianic acids possess the phthalide structure in the solid state, while in the aldehydic form they react solely in a medium that promotes ionization. In view of the fact that we carried out the reaction in ethyl acetate, a medium in which no ionization takes place, it is most probable that compounds of phthalide structure are formed.

We also condensed the amine (III) with p-acetylaminophenyl sulfochloride.

We prepared the aldehyde bisulfite derivatives of the amines (III) and (V) in order to synthesize compounds that were water-soluble.

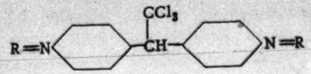
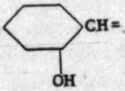
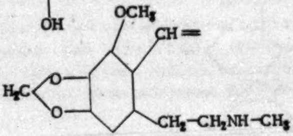
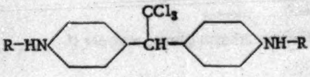
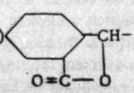
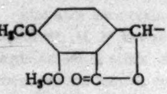
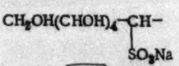
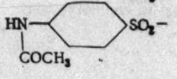
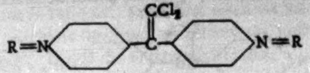
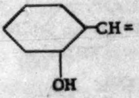
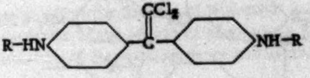
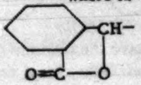
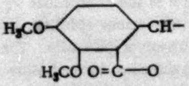
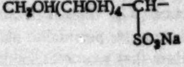
The compounds we have synthesized are listed in the following table.

EXPERIMENTAL

1,1,1-Trichloro-bis-(p-nitrophenyl)-ethane (II). 40 grams of 1,1,1-trichlorodiphenylethane, m.p. 62-64°, prepared by condensing chloral with benzene by means of sulfuric acid (d=1.84), was dissolved in 120 ml of chloroform. The solution was chilled to from -10 to -5° and thoroughly stirred and chilled while a mixture consisting of 160 ml of nitric acid (d= 1.5) and 40 ml of sulfuric acid (d=1.84) was slowly added. The acids were added at a temperature that did not exceed 0°. Then stirring was continued at room temperature for another 4 hours. The chloroform solution was removed, washed with water, and dried over calcium chloride. When the chloroform was driven off in vacuo, a viscous oil was left behind, which crystallized when a small amount of ether was added. The ether was filtered out, and the mass rewashed with ether, yielding 24-25 g of a substance. Crystallization of the latter from glacial acetic acid yielded 21-22 g of a substance with an m.p. of 164-165°, representing 40-42% of the theoretical yield. Recrystallization raised the melting point to 165-167°.

When 200 ml of sulfuric acid (d= 1.84) and 40 g of potassium nitrate were added to a chloroform solution of 1,1,1-trichlorodiphenylethane, the reaction resulted in the same yield, but one crystallization sufficed to secure a pure substance with an m.p. of 166-167°.

TABLE

Compounds synthesized from the amine (III)	Compounds synthesized from the amine (V)
 where R: 1)  2)   where R: 3)  4)  5) $NaO_3S{-}CH_2{-}$ 6)  $CH_2OH(CHOH)_4{-}\underset{SO_3Na}{CH}{-}$ 7) 	 where R: 8)   where R: 9)  10)  11) $NaO_3S{-}CH_2{-}$ 12)  $CH_2OH(CHOH)_4{-}\underset{SO_3Na}{CH}{-}$

1,1,1-Trichloro-bis-(p-aminophenyl)-ethane (III). The 1,1,1-trichloro-bis-(p-nitrophenyl)-ethane (II) was reduced catalytically as described in the literature [2]. The product was reprecipitated twice from its hydrochloride, its m.p. being 149-150°. The yield was 50% of the theoretical.

The 1,1,1-trichloro-bis-(p-nitrophenyl)-ethane was reduced by stannous chloride and hydrochloric acid in alcoholic solution, as described [4]. The reduction product was secured by diluting the reaction mass with water, neutralizing it with sodium acetate, and then extracting it with water. Difficulties were involved in this operation, inasmuch as vigorous agitation produced a stable emulsion. Only by means of slow and careful agitation, using large quantities of ether, were we able to extract the amine completely. The ether solution was processed with dilute hydrochloric acid (1:20). The acid solution was fractionally neutralized, a saturated solution of sodium acetate being added at first until the solution turned turbid, the precipitate thrown down being filtered out, and then more acetate being added until precipitation was complete. The resultant substance was dissolved in dilute hydrochloric acid and precipitated with sodium acetate. This yielded a substance with an m.p. of 149-151°, the yield being 90%. The amines synthesized by the two procedures were wholly identical and their mixed melting point exhibited no depression.

Found %: C 53.17; H 4.32; N 9.02; Cl 33.47. $C_{14}H_{13}N_2Cl_3$. Calculated %: C 53.33; H 4.12; N 8.88; Cl 33.80.

1,1,1-Trichloro-bis-(p-acetoaminophenyl)-ethane. When 1,1,1-trichloro-bis-(p-nitrophenyl)-ethane was catalytically reduced in acetic acid that contained a small percentage of acetic anhydride (b.p. 118-119°), and the product was neutralized, we obtained a substance that was insoluble in ether. The m.p. of the substance was 258-259° after crystallization from glacial acetic acid. When 1,1,1-trichloro-bis-(p-aminophenyl)-ethane (III) was acetylated with a mixture of acetic acid and acetic anhydride in pyridine, we obtained a substance with the same melting point (instead of 275° [2] and 245-250° [4]).

Condensing 1,1,1-trichloro-p,p'-diaminodiphenylethane (III) with aldehydes. The condensation products of the diamine (III) with aldehydes that are listed in the table were synthesized. The general procedure utilized in their synthesis was as follows: a mixture of equimolar solutions of the diamine and the aldehyde in ethyl acetate were heated to 65-70° for 2-3 hours. After the solution had cooled, a Schiff base slowly crystallized out. The yield was 80-90% of the theoretical.

As a rule, recrystallization lowered the melting points of the substance synthesized, so that we purified them by washing the synthesized compounds with alcohol, acetone, and ether.

1,1,1-Trichloro-bis-p,p'-(salicylideneaminophenyl)-ethane was synthesized from 1 mole of 1,1,1-trichloro-bis-(p-aminophenyl)-ethane (III) and 2 moles of salicylaldehyde, the yield being 75-80%. This yielded orange-yellow crystals with an m.p. of 185.5-186°. They were insoluble in water, sparingly soluble in alcohol and in ethyl acetate, and freely soluble in chloroform. They were purified by washing with alcohol and with ethyl acetate.

Found %: N 5.50; Cl 20.47. $C_{18}H_{21}N_2Cl_3O_2$. Calculated %: N 5.36; Cl 20.47.

1,1,1-Trichloro-bis-p,p'-(phthalidylaminophenyl)-ethane was synthesized by pouring together a solution of 1,1,1-trichloro-bis-(p-aminophenyl)-ethane (III) (1 mole) in ethyl acetate and a solution of phthalaldehydic acid (2 moles) in the same solvent. An abundant white precipitate settled out after 20-30 minutes of heating on a water bath. The yield was quantitative, and the m.p. 228-230°.

Found %: N 4.84; Cl 18.36. $C_{30}H_{21}N_2Cl_3O_4$. Calculated %: N 4.83; Cl 18.38.

The synthesized substance was insoluble in water or bicarbonate, sparingly soluble in alcohol, acetone, ethyl acetate, and soda, and soluble in alkali. The substance was soluble in bicarbonate after being precipitated from an alkaline solution by acetic acid.

1,1,1-Trichloro-bis-p,p'-(meconylaminophenyl)-ethane. When a benzene solution of 1 mole of 1,1,1-trichloro-bis-(p-aminophenyl)-ethane (III) was heated with 1 mole of opianic acid to 79-80° and then part of the benzene was driven off, a white powder was precipitated quantitatively, whose m.p. was 229-230° after washing with benzene, acetone, and ether.

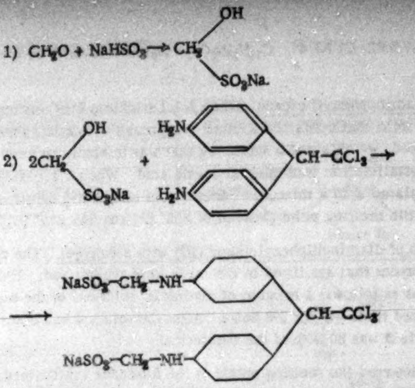
Found %: N 3.95; Cl 14.62. $C_{36}H_{29}N_2O_8Cl_3$. Calculated %: N 4.00; Cl 15.23.

The substance was insoluble in water, acetone, alcohol, ether, benzene and soda, and soluble in alkali. The substance just precipitated by acetic acid from an alkali solution and washed with water dissolved in bicarbonate.

1,1,1-Trichloro-bis-p,p'-(cotarnylideneaminophenyl)-ethane was synthesized by stirring a mixture of 1 mole of 1,1,1-trichloro-bis-(p-aminophenyl)-ethane (III) and 2 moles of cotarnine in ethyl acetate for 3-4 hours at room temperature and then allowing the solution to stand for 12-14 hours. A slightly pinkish powder was produced, its yield being almost quantitative. The substance was freely soluble in chloroform, though insoluble in water, alcohol, acetone, ether, benzene, and toluene. It was washed with alcohol and ether; its m.p. was 145.5-146°.

Found %: N 7.22; Cl 13.86. $C_{38}H_{39}N_4O_6Cl_3$. Calculated %: N 7.43; Cl 14.13.

1,1,1-Trichloro-bis-p,p'-(sodium salt of formaldehyde bisulfite-aminophenyl)-ethane. This reaction took place in two stages, as follows:


1) CH₂O + NaHSO₃ → CH₂(OH)SO₃Na.
2) 2CH₂(OH)SO₃Na + H₂N, H₂N, CH–CCl₃ →
NaSO₃–CH₂–NH–
NaSO₃–CH₂–NH–
CH–CCl₃

2 ml of a 31.8% solution of bisulfite and 0.6 ml of 37% formalin were placed in a three-necked flask fitted with a stirrer and heated on a water bath. Five to ten minutes later, after the absence of any excess formalin had been established by means of aniline water, a solution of 1 g of 1,1,1-trichloro-bis-(p-aminophenyl)-ethane (III) in 15 ml of alcohol was added, with stirring, to the flask, which was kept at 50-60°. Stirring was continued at 60-65° for 3 hours. Then the solution was decanted from the slight precipitate. When the solution was left to stand, crystals settled, which were filtered out and washed with alcohol. This yielded 1.2 g of a substance, its yield being approximately 75%. The substance contained 2 molecules of water of crystallization.

Found %: N 7.90; S 10.84. $C_{16}H_{15}O_6N_2S_2Cl_3Na_2 \cdot 2H_2O$. Calculated %: N 7.92; S 10.90.

The substance was soluble in water, producing a transparent, slightly yellow solution. The aqueous solution is partially hydrolyzed when it is allowed to stand for a few hours in the cold, a precipitate settling out.

1,1,1-Trichloro-bis-p,p'-(sodium salt of glucose sulfonate aminophenyl)-ethane. This was synthesized by adding 5.6 g of bisulfite (15 ml of a 37.8% solution) and 6 ml of water to 3.6 g of glucose. The resulting transparent solution was heated to 65-70° and stirred while a solution of 3.2 g of 1,1,1-trichloro-bis-(p-nitrophenyl)-ethane (II) in 50 ml of alcohol was added. Stirring and heating were continued for 4 hours. As the mixture cooled, a large quantity of an oily product settled to the bottom of the flask; it yielded a cream-colored powder when treated with absolute alcohol. The powder was suction-filtered, and 50 ml of absolute alcohol was added to the filtrate, yielding a little more of the same product. This yielded a total of 4.5 g of dry cream-colored powder. The yield was 50% of the theoretical. The substance was freely soluble in water. Concentrated aqueous solutions of the substance are faintly yellowish, while dilute solutions are absolutely colorless. The aqueous solution is unstable, hydrolyzing upon standing.

Found %: S 6.99; Na 5.25. $C_{26}H_{35}O_{16}N_2Cl_3S_2Na_2 \cdot 2H_2O$. Calculated %: S 7.24; Na 5.21.

1,1,1-Trichloro-bis-p,p'-(acetaminophenylsulfonamidophenyl)-ethane. 3 grams of p-acetylaminophenyl sulfochloride was gradually added at 0-2°, with constant stirring, to a solution of 2 g of 1,1,1-trichloro-bis-(p-aminophenyl)-ethane (III) in 10 ml of pyridine. After addition was complete, the reaction mass was heated to 40-45° for 3 hours, with stirring, and then allowed to stand overnight. The next morning the resultant solution was poured drop by drop, with stirring, into 1 liter of a 2% solution of hydrochloric acid, a flocculent pink precipitate (4 g) settling out. The substance was recrystallized from 50% alcohol, after which its m.p. was 223-224° (with decomposition). The substance was insoluble in water, though sparingly soluble in alcohol.

Found %: N 7.83; S 9.05; Cl 14.58. $C_{30}H_{27}O_6N_4S_2Cl_3$. Calculated %: N 7.90; S 9.03; Cl 15.04.

1,1-Dichloro-p,p'-bis-(nitrophenyl)-ethylene (IV) was synthesized by gradually adding 0.6 g of finely powdered potassium hydroxide to a suspension of 2 g of dinitrodiphenyltrichloroethane in 50 ml of alcohol at room temperature. The next day the precipitate was filtered out and washed with water. Crystallization from glacial acetic acid yielded 1.6 g of a substance with an m.p. of 172-173° (90% of the theoretical yield).

1,1-Dichloro-p,p'-bis-(aminophenyl)-ethylene (V). The 1,1-dichloro-p,p'-dinitrodiphenylethylene (IV) was readily reduced with molecular hydrogen, using Raney's nickel in glacial acetic acid at room temperature and atmospheric pressure, yielding an amine with an m.p. of 144-145°. The yield was 80% of the theoretical. The reduction of 1,1-dichloro-p,p'-bis-(nitrophenyl)-ethylene (IV) with stannous chloride and hydrochloric acid proceeded like the reduction of the 1,1,1-trichloro-bis-(nitrophenyl)-ethane (II), resulting in the production of dichloro-p,p'-bis-(aminophenyl)-ethylene (V) with an m.p. of 143-145°. The yield was 90% of the theoretical. The m.p. of the amine was 144.5-145° after recrystallization from dilute alcohol.

The amines produced by the two methods – catalytically and by reduction with stannous chloride and hydrochloric acid – were entirely alike, nor did their mixed melting point exhibit any depression.

1,1-Dichloro-bis-p,p'-(salicylideneaminophenyl)-ethylene was synthesized by adding 0.9 g of salicylaldehyde to a solution of 1 g of the unsaturated amine (V) in 20 ml of ethyl acetate. The solution was heated to 65-70° for 2 hours, its color rapidly turning orange. When it cooled 1.2 g of orange-colored crystals settled out. Evaporation of the filtrate yielded another 0.4 g of the substance. The yield of the pure product was 80% of the theoretical. The substance was soluble in chloroform, sparingly soluble in alcohol, ethyl acetate, and ether, and insoluble in water. Its m.p. was 191-193° after washing with alcohol and ether.

Found %: N 5.83; Cl 14.60. $C_{28}H_{20}O_2N_2Cl_2$. Calculated %: N 5.76; Cl 14.61.

1,1-Dichloro-bis-p,p'-(phthalidylaminophenyl)-ethylene. A solution of 1 g of phthalaldehydic acid in 30 ml of ethyl acetate was added to a solution of 1 g of 1,1-dichloro-p,p'-bis-(aminophenyl)-ethylene (V) in 10 ml of ethyl acetate, and the mixture was heated to 60-65° for 3 hours. The precipitated substance was dried and washed with ethyl acetate, alcohol, and ether, after which its m.p. was 250-251° (with decomposition). The yield totaled 5 g (90% of the theoretical).

Found %: N 5.28; Cl 12.97. $C_{30}H_{20}O_4N_2Cl_2$. Calculated %: N 5.15; Cl 13.07.

The substance was soluble in 2% alkali, though insoluble in 15% bicarbonate. The substance dissolved instantly in bicarbonate after it had been precipitated from an alkali solution by neutralization with acetic acid. Its m.p. was 218-220° (with decomposition).

1,1-Dichloro-bis-p,p'-bis-(meconylaminophenyl)-ethylene. A solution of 1.5 g of opianic acid in 30 ml of ethyl acetate was added to a solution of 1 g of 1,1-dichloro-p,p'-bis-(aminophenyl)-ethylene (V) in 30 ml of ethyl acetate, and the resultant solution was heated to 65-70° for 2 hours. A white precipitate was thrown down; it was filtered out and washed with ethyl acetate, alcohol, and ether, after which its melting point was 219-221°. The substance was soluble in alkali, and insoluble in bicarbonate.

Found %: N 4.32. $C_{34}H_{28}O_8N_2Cl_2$. Calculated%: N 4.22.

1,1-Dichloro-bis-p,p'-(sodium salt of formaldehyde bisulfite-aminophenyl)-ethylene was synthesized like the formaldehyde bisulfite derivative of 1,1,1-trichloro-bis-(p-aminophenyl)-ethane (III) at 70-75°, the yield being 80% of the theoretical. The substance was crystallized from 80% alcohol. Its aqueous solutions are transparent and unstable upon standing. The substance can be kept for 2-3 weeks in a dry, closed, dark place, rapidly darkening and decomposing when exposed to the open; it contains two molecules of crystallization water.

Found %: S 12.05; Na 8.53. $C_{16}H_{14}O_6N_2Cl_2S_2Na_2 \cdot 2H_2O$. Calculated %: S 11.72; Na 8.42.

1,1-Dichloro-bis-p,p'-(sodium salt of glucosesulfonate-aminophenyl)-ethylene was synthesized like the glucoside sulfonate derivative of 1,1,1-trichloro-bis-(p-aminophenyl)-ethane. It was a faintly cream-colored powder after it had been processed with absolute alcohol. The yield was 60% of the theoretical. The substance was freely soluble in water. Concentrated solutions are slightly yellowish, dilute solutions being colorless. Aqueous solutions are unstable when stored.

Found %: N 3.12; S 7.63; Na 5.45. $C_{26}H_{34}O_{16}N_2Cl_2S_2Na_2 \cdot 2H_2O$. Calculated %: N 3.30, S 7.55; Na 5.43.

SUMMARY

1. A method has been developed for nitrating 1,1,1-trichlorodiphenylethane.

2. 1,1,1-trichloro-p,p'-diaminodiphenylethane (III), with an m.p. of 149-150°, has been synthesized, the yield being 90% of the theoretical.

3. Reducing 1,1,1-trichloro-p,p'-dinitrodiphenylethane and 1,1-dichloro-p,p'-dinitrodiphenylethylene in glacial acetic acid that contained acetic anhydride produced high yields of the acetyl derivatives of the respective amines.

4. The structure of the synthesized nitro amino compounds has been established as that of p,p' substitution derivatives of diphenyltrichloroethane and diphenyldichloroethylene.

5. Twelve compounds, four of which are water-soluble, have been secured from 1,1,1-trichloro-p,p'-diaminodiphenylethane and 1,1-dichlorodiaminodiphenylethylene and have been identified.

6. Contrary to foreign findings that 1,1,1-trichloro-p,p'-diaminodiphenylethane and its ethylene derivative are highly active tuberculostatically, these compounds were found to be only slightly active.

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Received March 10, 1950.

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ALKYLATION OF AROMATIC COMPOUNDS IN THE PRESENCE OF PHOSPHORIC ACID

THE POLYALKYLATION OF PHENOL

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In the alkylation of aromatic compounds the principal objective, as a rule, is the synthesis of monoalkyl derivatives. The reason for this is that more research has been done on monoalkylated products, and they are, therefore, more widely used. Moreover, research on the process and on the reaction products is itself simpler. This also holds true of the alkylation of phenols. It is asserted in some papers that di- and trialkylphenols have been obtained, but there is only one paper specially devoted to the synthesis and a study of the properties of some trialkylphenols [1].

We have made a study of the polyalkylation of phenol with n-butyl and isobutyl alcohols in the presence of phosphoric acid. In our laboratory we have more than once shown [2] that phosphoric acid is superior to other condensing agents in the alkylation of phenol by alcohols. When equimolecular quantities of the alcohol and phenol are used in condensation with phosphoric acid we get satisfactory yields of pure monoalkylated phenols, whereas many other catalysts produce a mixture of products of varying degrees of substitution. By using phosphonic acid we hoped to ascertain whether two or three alkyl groups can be introduced during alkylation as desired. We took the corresponding quantities of alcohol and phenol to guide the reaction along the desired course, besides increasing the intensity and duration of the heating.

In the condensations with n-butyl alcohol we managed to find the conditions required for obtaining a compound with the desired degree of substitution as the principal product. We used 2 moles of n-butyl alcohol and 400 ml of phosphoric acid (d = 1.86) per mole of phenol to introduce 2 butyl groups; heating lasted 11 hours at 130-150°. The aggregate yield of disubstituted products (dibutylphenol and the butyl ether of butylphenol) was 70% of the theoretical. We accordingly used 3 moles of the alcohol and 600 ml of phosphoric acid to introduce three groups, heating to 140-160° being continued for 23 hours. The yield of trisubstituted products was 70% of the theoretical.

The reaction with isobutyl alcohol did not proceed nearly as satisfactoriliy under these conditions, although isobutyl alcohol enters into condensation reaction more readily, as we know. This is apparently due to the fact that the alkylation reaction is paralleled by the reverse reaction: dealkylation, the two reaction rates being governed by the temperature. As the temperature is raised, the rate of alkylation rises, though the rate of dealkylation rises still faster when a certain temperature is exceeded. When the temperature is kept low, we can expect to keep the reverse reaction to a minimum. As a matter of fact, we were able to improve the yield of polybutylphenols somewhat by lowering the temperature. The reactions with isobutyl alcohol were run with the same reagent proportions and heating time as those used for n-butyl alcohol, but the reaction temperature was varied. Dialkylation was performed at 140°, the yield of dialkylated products totalling 45% of the theoretical. Trialkylation at 110-120° yielded 37% of tributylphenol, whereas performing this same reaction at 140-160° yielded only 25% of the trisubstituted product. In all the isobutyl alcohol condensations a high percentage of a monosubstituted product was formed, in addition to the polybutylphenols. Cutting the heating time to 8 hours (125-135°) results in the monosubstituted product predominating in the reaction products, with no tributylphenol present at all. By way of making a more detailed study of the polyalkylation process, we tried to perform this reaction step by step, in the thought that when the alkyl groups were introduced gradually the reaction would be smoother, yielding the desired product completly. With this as our objective we condensed p-tert-butylphenol with isobutyl alcohol. But when the second alkyl group was introduced, we found that the reaction was not as smooth as when the first group was added. This is most likely due to parallel dealkylation.

According to the findings of Stillson and his associates [1], trialkylphenols that contain tertiary radicals do not dissolve at all in aqueous alkalies or in a solution of potassium hydroxide in methanol. Trialkylphenols that contain secondary radicals are insoluble in aqueous solutions of alkalies, but do dissolve in alcoholic solutions of potassium hydroxide. The solubility of dialkylphenols in these solutions depends upon the nature of the alkyl groups and their positions. We utilized aqueous solutions of alkalies of varying concentrations to separate the dialkylphenols from the phenol ethers. The condensation products of n-butyl alcohol can be readily separated by means of strong (20-30%) solutions of alkali. Tributylphenol is wholly insoluble in such a solution. With the isobuytl alcohol it is best to use dilute alkali solutions (5-10%).

In the light of the conditions governing their recovery the trisubstituted products might be regarded as a mixture of tributylphenol with butyl ethers of the dibutyl-phenols. Determination of the hydroxyl groups indicated, however, that the substances were 100% phenols. It is evident that distillation entailed the isomerization of the phenol ethers to aklyl phenols.

The di-and tributylphenols were obtained as oily liquids that did not crystallize upon standing, which was due, apparently, to the formation of a mixture of isomers with differing radical structures. It is very difficult to purify the di- and tributylphenols, since they are dealkylated appreciably when distilled, even in vacuo. Analysis of the collected fractions indicates that substances of a lower degree of substitution are present.

We did not investigate the phenol ether fractions, since they were partially isomerized to the corresponding alkylphenols when distilled.

EXPERIMENTAL

The phosphoric acid (d = 1.86) utilized in our condensations was prepared by evaporating commerical phosphoric acid with some nitric acid in a platinum cup. After the acid had cooled, it was diluted with distilled water to the required strength. The use of glass or porcelain vessels in evaporating the phosphoric acid contaminates it with impurities that diminish its activity.

Condensation was performed in a three-neckedflask, using mechanical stirring. A mixture of phenol and phosphoric acid was heated to the required temperature, and the alcohol was added from a dropping funnel, after which stirring and heating were continued. The reaction temperature was checked by means of a thermometer immersed in the reaction mixture.

When the reaction was over, the mixture was diluted with water, the upper layer being removed and processed a few times with an alkali solution. The alkali solutions were combined, and the phenols extracted from them by the action of hydrochloric acid. The precipitated phenols were washed with water until their reaction was neutral, dried over calcium chloride, and distilled.

The portion of the alkylation products (the tributylphenols and the butyl ethers of the mono- and dibutylphenols) that was insoluble in the alkali was likewise washed with water until its reaction was neutral, dried over calcium chloride, and fractionated. Broad fractions were collected, the yield being calculated in terms of these crude products. The corresponding fractions of similar condensations were combined together and repeatedly distilled in vacuo and at ordinary pressure. The isolated narrow fractions of phenols constituted mixtures of isomers. They were identified only by their analyses and their constants, inasmuch as no derivatives of di- and tributylphenols can be prepared under ordinary conditions. No investigation was made of the nonphenolic part of the condensation products.

Condensation of phenol with n-butyl alcohol. The condensation conditions and results are listed in Table 1.

Redistillation of the 245-270° phenolic fraction yielded the dibutylphenol (a mixture of isomers).

B.p. 257-265°; d_4^{21} 0.9445; n_D^{21} 1.5100; MR_D 65.08; calculated 64.78.

0,1302 g substance: 0.3868 g CO_2; 0.1179 g H_2O. 0.2188 g substance: 30.2 ml CH_4 (29°, 718 mm).
Found %: C 81.02; H 10.06; OH 8.40, $C_{14}H_{22}O$. Calculated %: C 81.55; H 10.68; OH 8.25.

The 270-290° fraction yielded the tributylphenol (a mixture of isomers).

B.p. 275-279°; d_4^{21} 0.9373; n_D^{21} 1.5074; MR_D 83.3; calculated 83.25.

0.0908 g substance: 0.2745 g CO_2; 0.0896 g H_2O. 0.2126 g substance: 25.9 ml CH_4 (29°, 718 mm): Found %: C 82.45; H 10.96; OH 7.45. $C_{18}H_{30}O$. Calculated %: C 82.44; H 11.45; OH 6.49.

TABLE 1

Results of Condensing *n*-Butyl Alcohol with Phenol

Condensation number	Original substances			Temperature	Time hours	Product yield			
						From the alkali solution		Portion insoluble in alkali	
	Phenol	Alcohol	Ml of H_3PO_4			Butylphenol, b.p. 220-245°	Dibutylphenol b.p. 245-270°	Butyl ether of butylphenol, b.p. 245-270°	Tributylphenol b.p. 270-295°
1	23.5 g (0.25 mole)	37 g (0.5 mole)	100	130-150°	11	9.5 g (9%)	14.5 g (28 %)	21.6 g (42 %)	4.6 g (7 %)
2	23.5 g (0.25 mole)	55 g (0.75 mole)	150	140-160	23	–	–	–	46 g (70%)

TABLE 2

Condensation No.	Original substances			Temperature	time hours	Product yield					
						From the alkali solution			Portion insoluble in alkali		
	Phenol	Alcohol	Ml of H_3PO_4			Butylphenol, b.p. 220-245°	Dibutyl-phenol, b.p. 245-265°	Tributyl-phenol b.p. 265-280°	Butyl ether of phenol 220-245°	Butyl ether of dibutyl phenol, b.p. 245-265°	Tributyl-phenol b.p. 265-280°
1	47 g (0.5 mole)	74 g (1 mole)	200	135-145°	11	8 g (10.7%)	33 g (32 %)	7.5 g (6%)	–	13 g (12.6%)	8.9 g (7 %)
2	23.5 g (0.25 mole)	55 g (0.75 mole)	150	125-135	8	17 g (46 %)	–	–	6.3 g (17 %)	17.5 g (34 %)	–
3	23.5 g (0.25 mole)	55 g (0.75 mole)	150	140-160	22	5.1 g (13.6%)	15.7 g (30.5%)	4.6 g (7%)	4.3 g (11.5%)	4.0 g (7.8 %)	11.5 g (17.6 %)
4	23.5 g (0.25 mole)	55 g (0.75 mole)	150	110-120	22	6.5 g (17.4 %)	4.5 g (8.7 %)	–	3.3 g (9 %)	6.0 g (11.6 %)	24.2 g (37%)

The fraction constituting the butyl ether of butyl phenol dissolved partially in potassium hydroxide after distillation, indicating that isomerization to dibutylphenol had taken place.

Condensing phenol with isobutyl alcohol. The condensation conditions and results are listed in Table 2.

The 220-245° phenolic fractions crystallized in part upon standing. The precipitated crystals had an m.p. of 99° after recrystallization from water, which is the m.p. of *p-tert*-butylphenol.

Redistillation of the 245-265° phenolic fractions yielded the dibutylphenol (a mixture of isomers).

B.p. 255-262°; d_4^{22} 0.9538; n_D^{22} 1.4965; MR_D 63.16; calculated 64.78.

0.1130 g substance: 0.3366 g CO_2; 0.1024 g H_2O. Found %: C 81.24; H 10.07; $C_{14}H_{22}O$. Calculated %: C 81.55; H 10.68.

Distillation of the 265-280° fractions yielded a product with a b.p. of 275-280°; d_4^{22} 0.9488; n_D^{22} 1.4965. Analysis of this product indicated that it consisted largely of low-molecular phenols.

SUMMARY

1. The polyalkylation of phenol by *n*-butyl and isobutyl alcohols in the presence of phosphoric acid

has been investigated.

2. In the case of n-butyl alcohol the conditions have been discovered that make it possible to introduce two or three butyl groups into the phenol molecule (with yields up to 70% of the theoretical). The reaction is not complete when isobutyl alcohol is used, owing to the parallel dealkylation that takes place.

3. The condensations yield a mixture of alkylphenols and phenol ethers. The di- and tributylphenols are partially dealkylated during distillation.

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Received June 13, 1950.

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THE ALKYLATION OF AROMATIC COMPOUNDS BY ALCOHOLS IN THE PRESENCE OF ALUMINUM CHLORIDE

XV.* THE ALKYLATION OF BENZENE IN A CONTINUOUS-ACTION APPARATUS

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In some recent reports by A. V. Topchiev and his associates [1] the authors have described the alkylation of benzene and of saturated hydrocarbons with the new catalyst $BF_3 \cdot H_3PO_4$ in a continuous-action apparatus. This alkylation method cuts down the formation of polyalkyl derivatives; in our reactions using $AlCl_3$ we may also look forward to an appreciable diminution of the side reactions of cleavage and isomerization of the alcohol radicals as the result of the action of the $AlCl_3$ or of its coordination compounds. Changing the apparatus described by A. V. Topchiev, and his associates [1] somewhat, we used it to alkylate benzene with isopropyl, *n*-butyl, and ethyl alcohols reactions which had been previously investigated in our laboratory. In the apparatus reactor there gradually accumulated a heavy, oily "lower layer" that contained $AlCl_3$, the products of its interaction with alcohol, and various by-products (polyalkylated derivatives, olefins and others) in the shape of coordination compounds with $AlCl_3$. Rapidly removing the normal reaction products from this layer ought to improve the results of alkylation. By using syphoning from the reactor to the distilling flask, we achieved complete separation of the reaction mixture from the lower layer. But when the excess benzene was driven off from the decanted colored mixture, an oily lower layer again separated out. Still, we believe that the influence of the excess $AlCl_3$ and of the lower layer has been greatly reduced in the experiments we have carried out.

According to our earlier findings [2], alkylating benzene with isopropyl alcohol yielded up to 70% of alkylbenzenes, though the mixture contained a large percentage of di- and polyisopropylbenzenes. Condensation in the apparatus with 0.6 mole of $AlCl_3$ per mole of C_3H_7OH yielded 66.5% of alkylbenzenes; the mixture of crude products contained almost no high-boiling fractions, proving to be pure cumene.

In our previous experiments [2] on the alkylation of benzene with *n*-butyl alcohol, we secured negligible yields of butylbenzene. The reactions were carried out with only 1.2-2 moles of $AlCl_3$ per mole of the alcohol at temperatures above 100°; under these conditions most of the alcohol underwent cleavage. When small quantities of $AlCl_3$ were used on a water bath, no perceptible yields of butylbenzene were obtained. We then ran a new series of tests on the alkylation of *n*- C_3H_7OH in the apparatus. We varied the quantity of $AlCl_3$, the temperature, and the order in which the reagents were added. We found that at least 1.2 moles of $AlCl_3$ were required per mole of the alcohol, as had been demonstrated earlier [3]; however, the reaction takes place in the apparatus at 75-80°, yielding about 35% of the theoretical (based on the alcohol used) of the monobutylbenzenes. The reaction mixture contains practically no polyalkylbenzenes. We made an approximate determination of the amount of unreacted *n*-butyl benzene in the wash waters by measuring the refractive index; subsequent calculation indicated that the butylbenzene yield was 60% of the theoretical, based on the reacted *n*-butylbenzene. The resultant butylbenzene proved to be a mixture of isomers, with *sec*-butylbenzene predominating.

When we alkylated benzene with ethyl alcohol in the past [4], we always obtained a high yield (as high as 90% of the theoretical) of a mixture of hydrocarbons, the ethylbenzene yield never exceeding 35-40%, di- and polyethylbenzenes predominating. This result was obtained when we used 2 moles of $AlCl_3$ per mole of alcohol and heated the mixture for 10 hours on an oil bath (120-130°). Alkylation tests with ethyl alcohol run in the apparatus indicated that the specified quantity of $AlCl_3$ is actually required to secure high product yields. The reaction proceeds faster and at a lower temperature in the apparatus. Heating the mixture for 2 hours on a water bath yielded 85% of the theoretical yield of alkylbenzenes; the mixture of reaction products yielded a total of 25-30% of the theoretical yield of ethylbenzene, the bulk of the product consisting of di- and polyethylbenzenes. In these condensations we always observed the formation within the reactor of an oily lower layer, which contained polyethylbenzenes, as was proved by a special test. It is evident that the alkylation products are selectively extracted by the lower layer [5], under our reaction conditions, resulting in the specified condensation results. Hence, there is no advantage to be gained by ethylating benzene in the device over the usual method of performing these condensations, as far as the composition of the reaction products is concerned.

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*For Communication see J. Gen. Chem., 18, 106 (1948).

EXPERIMENTAL

The following modifications were made in the apparatus described by A. V. Topchiev and his associates [1]. The reactor was fitted with an auxiliary tube for gradually supplying the $AlCl_3$. The motor-driven stirrer was replaced by a magnetic stirrer. The overflow tube was made of two glass sections connected together by rubber tubing fitted with a clamp; the end of the tube that was lowered into the distilling flask was drawn out to a narrow tip (2 mm diameter); all this made it possible to regulate the overflow of the transparent reaction mixture better.

Benzene-isopropyl alcohol. 43 grams (0.32 mole) of $AlCl_3$ was gradually added to a mixture of 150 ml of benzene and 30 g (0.5 mole) of C_3H_7OH in the reactor. Then the mixture was heated on a water bath (75°) for 2 hours and left to stand at room temperature for 12 hours. Then we began to drive the benzene (200 ml) out of the distilling flask. At the same time that the benzene entered the mixture of products was decanted from the reactor to the distilling flask; this took 2 hours.

After the usual processing, we obtained the following fractions: 2.3 g at 80-145°; 37.6 g at 145-202°; and 1.2 g of residue. Redistillation of the first two fractions yielded 37 g of cumene, with the following constants [6]: b.p. 148-152° (730 mm); d_4^{20} 0.8731; n_D^{20} 1.4942.

Benzene-n-butyl alcohol. We took: 300 ml of benzene, 25 g (0.33 mole) of n-C_4H_9OH, and 55 g of $AlCl_3$ (0.42 mole). After the $AlCl_3$ had been added, the mixture was heated to 75° for 3 hours; then we began to siphon from the reactor to the distilling flask and drive the benzene into the reactor (3 hours). The fractions collected were: 15.5 g at 140-180° (butyl-benzene, 34% of the theoretical); 0.7 g at 180-190°; and 1.3 g of residue.

The reaction mixture was thoroughly washed with an excess of acidulated water to determine the percentage of unreacted butyl alcohol. The collected wash waters were alkalinized and then brought to 1 liter. Then the refractive index of a distilled portion (100 ml) of the wash waters was determined. It was found to be n_D^{25} 1.3350, equivalent to some 1.1% of n-butyl alcohol (determined in a control experiment), whence the unreacted n-C_4H_9OH totaled 11 g; hence, the butylbenzene yield was about 60%, based on the reacted n-C_4H_9OH.

Repeated distillations of the crude butylbenzene yielded a 168-170° (730 mm) fraction; d_4^{20} 0.8603; n_D^{20} 1.4912; MR_D 45.14.

These fractions had constants that approximated those of sec-butylbenzene [6,7]; the slight deviation from the values in the literature is evidently due to the presence of a slight amount of n-butylbenzene. We determined the approximate percentage of n-butylbenzene graphically, using the data in the refractive indexes of the isomeric butyl-benzenes. The sec-butylbenzene totaled about 15%. Lastly, we secured an acetamino derivative with an m.p. of 127° [7] to identify the sec-butylbenzene.

Benzene-ethyl alcohol. We used: 300 ml of benzene, 16 g (0.33 mole) of alcohol, and 87 g (0.66 mole) of $AlCl_3$. The mixture was heated on a water bath for 2 hours. Syphoning lasted 3 hours. The lower layer was separated from the benzene layer for processing and decomposed separately with water. The following fractions were collected: from the benzene layer: 0.2 g at 90-110°; 3.2 g at 110-150°; and 0.2 g of residue; from the lower layer: 5 g at 110-150°; 7.1 g at 150-200°; 32 g at 200-250°; and 4.3 g of (crystalline) residue.

Repeated distillations of the 110-150° fraction yielded ethylbenzene with a b.p. of 134-135° (730 mm); d_4^{20} 0.8675; n_D^{20} 1.4959.

SUMMARY

1. A study has been made of the alkylation of benzene with alcohols and $AlCl_3$ in a continuous-action apparatus.

2. Isopropyl alcohol yielded cumene, the yield being 60% of the theoretical.

3. This method of condensation made it possible for the first time to effect the butylation of benzene with n-C_4H_9OH with a satisfactory yield (as high as 60% of the theoretical, based on the reacted alcohol).

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Received October 21, 1950

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* See Consultants Bureau translation, p. a-649.

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[7] [illegible]

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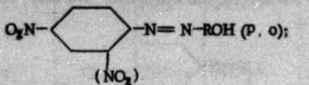
THE RELATIONSHIP OF THE STRUCTURE OF HYDROXYAZO DYES TO THEIR ABILITY TO CHANGE COLOR AT THE SURFACE OF MAGNESIUM HYDROXIDE

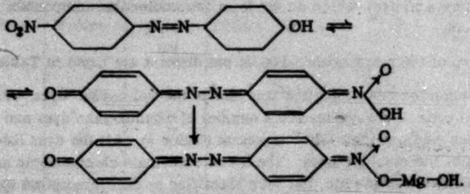
L. M. Kulberg

Among the reagents for magnesium there is a large group of hydroxyazo dyes, all of which change color at the surface of magnesium hydroxide characteristically at the instant of its formation. The hydroxyazo dyes that exhibit this reaction can be divided into two groups. One group includes the p-nitro- and o-nitrohydroxyazo dyes with the following general formula:



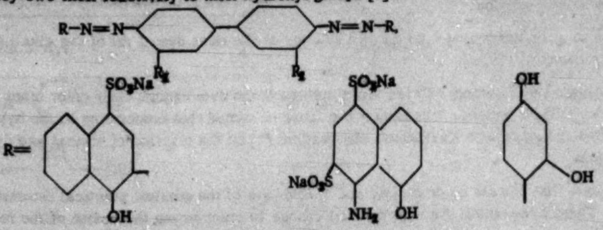
the other including the hydroxyazo dyes that do not contain a nitro group (or else have it at the meta position).

The interaction of the first group of dyes with magnesium hydroxide has been exhaustively investigated by us previously [1]; we found that the reaction involves the stabilization of the isonitro form of the dye [2] at the surface of the magnesium hydroxide as follows:



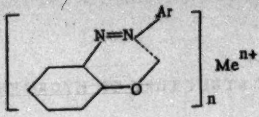
As for the second group, practially no research is found in the literature on their interaction with magnesium hydroxide [3,4].

The author, who has pointed out that dyes of the first type can be utilized as reagents for magnesium, believes that they owe their reactivity to their hydroxyl groups [5]:

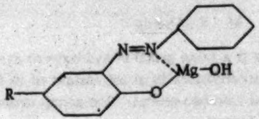


R_2 = H, CH_3, OCH_3.

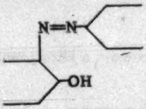
We know that the o-hydroxyazo dyes form inner coordination compounds with metals very readily, with the aryl group in the trans position to the azo group [6]:



This led us to conjecture that the interaction of this group of dyes with magnesium hydroxide entails the formation of an intramolecular compound [3], such as:



followed by its fixation at the surface of the magnesium hydroxide. We may, therefore, suppose that o-hydroxyazo dyes of the following general formula:



must be reactive to the magnesium ion (that is, change color characteristically at the surface of the $Mg(OH)_2$ at the instant the latter is formed).

Obviously, the p-hydroxyazo dyes, which do not form intramolecular compounds, should not color $Mg(OH)_2$ under these conditions.

The results of our tests of the p-hydroxyazo dyes at our disposal are listed in Table 3.

To prove that our assumption concerning the structure of the hydroxyazo dyes, which ensures their reactivity with $Mg(OH)_2$, was correct, we synthesized a number of o-hydroxyazo dyes and tested their ability to change color in an alkaline medium when Mg^{2+} is present (Table 1). All the dyes listed in the table were synthesized 1) and identified by the usual methods. The dyes that contain chromotropic and H acids as azo components were not isolated in the solid state, but were identified by their absorption spectra.

In the reactions we used 0.1% alcoholic solutions of the dyes (an aqueous-alcoholic solution being used for a dye that was insoluble in alcohol), a 1% solution of chemically pure magnesium sulfate heptahydrate, and a 1N solution of sodium hydroxide (a 0.1 N solution of sodium hydroxide being used when testing dyes that contain chromotropic acid residues). 0.25 ml of the dye solution and 1 ml of the alkali solution were added to 1 ml of the magnesium sulfate solution.

We used a solution containing 0.25 ml of a solution of the same dye, 1 ml of the alkali solution, and 1 ml of water as a control.

As we see from these findings, all the tested o-hydroxyazo dyes change their color more or less pronouncedly when $Mg(OH)_2$ is present at the instant the latter is formed thus conforming to the hypothesis advanced. These findings agree with Kuznetsov's observations [4] on the reaction of several azo dyes with Li^+, Ca^{2+}, and Mg^{2+} ions.

The azo dyes that contain chromotropic and H acids are of the greatest practical interest as reagents for magnesium. These dyes exhibit the most marked change in color during the course of the reaction.

Thus, among the hydroxyazo dyes that can change color at the surface of $Mg(OH)_2$ we encounter two functional-analytical groups that give rise to reactions with the Mg^{2+} in an alkaline medium that are of the same type externally speaking, but differ fundamentally as far as their mechanisms are involved:

---

1) The diazo and azo components were always coupled in a slightly alkaline medium.

TABLE 1

Color of Alkaline Solutions of o-Hydroxyazo Dyes with and without Magnesium Salts

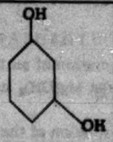
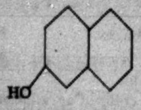
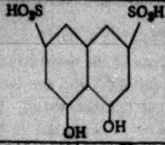
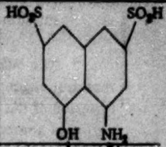
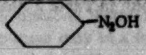
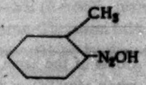
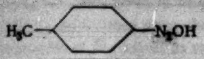
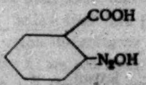
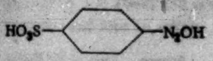
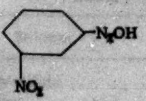
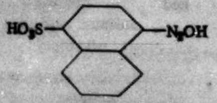
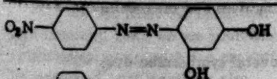
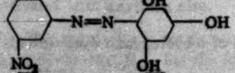
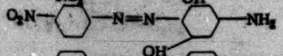
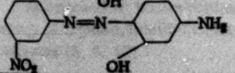
Diazo component	Azo Component							
								
	K 1)	M^{2+} 2)	K	Mg^{2+}	K	Mg^{2+}	K	Mg^{2+}
	Pink	Yellow	Pink	Yellow	—	—	—	—
	— 3)	—	Pink	Brown	Pink	Sky-blue	Pink	Violet
	Red	Chest-nut	Yellow	Orange	Yellow	Orange	Blue	Violet
	Pink	Yellow	Yellow	Pink	Pink	Crimson	Pink	Crimson
	Yellow	Lilac-red	Yellow	Orange	Pink	Violet	Red	Violet
	Yellow	Lilac-red	Red	Orange	Red	Blue	Blue	Lilac
	Orange	Crimson	Orange	Crimson	Red	Blue	Pink	Violet

TABLE 2

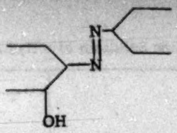
Effect of the Structure of o-Hydroxyazo Dyes Upon the Mechanism of the Reaction with Mg^{2+}

Formula of dye	Color of a weakly alkaline solution of the dye	Color of the same solution in the presence of: Mg^{2+}	Color of the same solution in the presence of: Acetone
	Red-brown	Blue	Blue
	Pink-yellow	Lilac-red	Pink-yellow
	Lilac-red	Blue	Blue
	Yellow	Lilac-red	Yellow

1) Color of the control solution. 2) Color when magnesium salt is present. 3) Dye not tested

1) $HO-Ar-N{=}N-Ar'-NO_2$
(p, o) (p, o)
Intramolecular rearrangement with stabilization of the isonitro form at the $Mg(OH)_2$ surface

2)

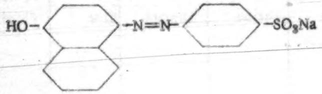
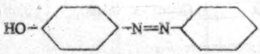
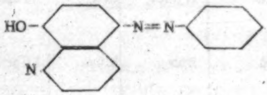
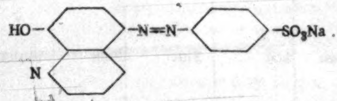


Formation of an inner complex salt which is stabilized at the $Mg(OH)_2$ surface

The behavior of the o-hydroxyazo dyes that are reagents for Mg^{2+} with acetone is a criterion of the reaction mechanism. If the action of acetone causes a change in the color of an alkaline solution of the dye, like that occurring when a magnesium salt is present, it is an indication of the isomerization of the dye to the isonitro form. The absence of this effect is evidence that an intramolecular compound has been formed. The data set forth in Table 2 illustrates the foregoing.

TABLE 3

Nature of the Interaction of p-Hydroxyazo Dyes with Mg^{2+} in an Alkaline Medium

Formula of the dye	Color of the alkaline solution of the dye	Color of the same solution when $Mg(OH)_2$ is present
	Red	Red
	Brown	Brown
	Brown .	Brown
	Red	Red

SUMMARY

1. It has been shown that hydroxyazo dyes that do not have a nitro group in the para or ortho position to the azo group react with Mg^{2+} in an alkaline medium only when they have a hydroxy group in the ortho position to the azo group.

2. The hypothesis is put forward that the reaction between the foregoing dyes and magnesium salts in an alkaline medium involves the formation of inner complex salts.

3. This hypothesis has been confirmed by a study of the reaction of several synthesized dyes with magnesium salts in an alkaline medium.

4. A criterion is given for establishing the mechanism of the reaction of o-hydroxyazo dyes with Mg^{2+} in an alkaline medium.

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Received July 16, 1950.

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THE DISSOCIATION OF HEXAPHENYLETHANE AND SIMILAR COMPOUNDS IN SOLUTIONS

D. A. Pospekhov

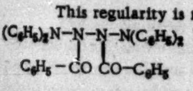
Waters [5] has expressed the following opinion on the dissociation of hexaphenylethane and related compounds in solutions: "Formation of neutral radicals when bonds in organic compounds are dissociated may be expected to occur only in a few solvents with low dielectric constants," and he has asserted that such solvents as ethyl alcohol ($\varepsilon = 25$), nitrobenzene ($\varepsilon = 36$), and the like, promote ionization. This view constitutes a parallel to the Nernst-Thomson rule in the electrochemistry of solutions: the higher the dielectric constant of a solvent the greater will be its dissociating power [3,7,11,12]. (Waters did not notice this parallel). The rule has been discussed frequently [1-4, 6, 7, 13-15]. The limits of its applicability have been commented upon. Some authors have considered the rule to be false [2, 3, 6]. In Walden's works on nonaqueous solutions of electrolytes [13-15], he insisted upon the correctness of the rule, but in his book on free radicals [17] he did not discuss the formation of the latter as related to the ε of the solvent.

We shall show that the experimental data now available do not bear out the cited opinion of Waters. The table below lists data [18] on hexaphenylethane, supplemented by information on the ε of the solvent. The order in which the solvents are listed in the original paper has been modified somewhat: they are here grouped in classes. As we see from the table, the heats of dissociation of all the solvents, even including proprionitrile ($\varepsilon = 27.7$), are about the same; hence there are no grounds for the belief that free radicals are formed in some solvents and ions in others.

TABLE

Solvent	Dissociation constant $K \cdot 10^4$ at 20°	Heat of dissociation Q, kcal.	Solvent's, ε
Hydrogen sulfide	19.2	11.0	2.64
Chloroform	6.9	10.5	5.05
Ethylene bromide	3.9	11.4	6.3
Proprionitrile	1,2	11.1	27.7
Benzene	4.1	11.3	2.3
Bromobenzene	3.7	11.5	5.4
Acetophenone	1.70	11.5	18.3
Ethyl benzoate	1.67	12.0	6.2
Dioxane	2.5	11.6	2.2

We see from the table that in aliphatic solvents the lower the ε of the solvent, the higher its dissociation constant, i.e., we see somewhat of a contradiction to what Waters asserted. The same rule holds in the aromatic solvents, with the exception of acetophenone. Dioxane, as the sole heterocyclic compound, cannot be compared with anything else.

This regularity is not fortuitous, inasmuch as we know of similar facts: tetraphenyldibenzoyltetrazane  $(C_6H_5)_2N-\underset{C_6H_5-CO}{N}-\underset{CO-C_6H_5}{N}-N(C_6H_5)_2$ has the following values of $K \cdot 10^4$ at -18°: 2.75 in ether ($\varepsilon = 4.3$), 2.36 in chloroform ($\varepsilon = 5.05$); and 1.48 in acetone ($\varepsilon = 21.4$) [8].

As opposed to Waters' opinion, solutions of hexaphenylethane in nitrobenzene are nonconductors [10]. (Solutions of triphenylmethyl in liquid sulfur dioxide ($\varepsilon = 15.6$) are conductors, owing to the formation of salt-like solvates [5, 6, 17].

When the degree of dissociation of di-p-benzylhydroxyhexaphenylethane and di-p-methoxyhexaphenylethane was determined cryoscopically in benzene ($\varepsilon = 2.3$) and in nitrobenzene ($\varepsilon = 36$), it was found that the former compound is more strongly dissociated in benzene than in nitrobenzene, while the latter exhibits the opposite behavior [9]. Let us cite, by way of example, several figures: $\alpha = 0.346$ when 2.31 g of the first compound is used per 100 g of benzene, while $\alpha = 0.329$ when 2.20 g is used per 100 g of nitrobenzene; $\alpha = 0.238$ when 2.89 g of the second compound is used per 100 g of benzene, and $\alpha = 0.295$ when 2.88 g are used per 100 g of nitrobenzene. The thermal factors of dissociation are very much alike in both solvents, owing to the proximity of their melting points (5.3° and 5.8°, respectively).

As we see from the foregoing, there is no support for Water's opinion. It must be borne in mind, however, that very little work has been done on these compounds, especially as far as solvents with high values of ε are concerned. Further research should indicate whether any regular pattern of behavior analogous to the Nernst-Thomson rule can be established for even some of the solutions discussed here.

SUMMARY

Existing data on the dissociation of hexaphenylethane and similar compounds in solutions are discussed. It is shown that these data give no evidence of the existence of any direct parallelism between the degrees of dissociation of these substances and their character (dissociation into neutral radicals or dissociation into ions), on the one hand, and the dielectric constants of the solvents on the other.

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Received August 17, 1950

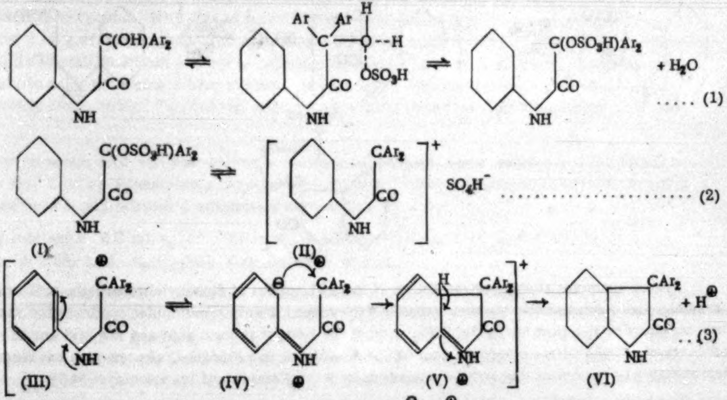
Kiev Institute of Forestry

THE N-ARYL AMIDES OF HYDROXY CARBOXYLIC ACIDS AND THEIR CONVERSION INTO HETEROCYCLIC COMPOUNDS

XV. THE MECHANISM INVOLVED IN THE INTRAMOLECULAR CONDENSATION OF N-ARYL AMIDES OF HYDROXY CARBOXYLIC ACIDS

P. A. Petyunin

Discussion of the mechanism involved in the intramolecular condensation of aryl amides of hydroxy carboxylic acids is facilitated by the fact that some of the essential factors of this problem have been considered by us previously. The mechanism involved in the intramolecular condensation of the aryl amides of hydroxy carboxylic acids may be represented as follows:

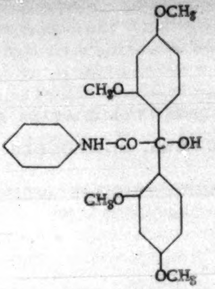


$SO_4H^{\ominus} + H^{\oplus} \rightarrow H_2SO_4$ .... (4)

We have noticed more than once that intramolecular condensation does not involve the direct splitting out of elements of water from the aryl amide molecule, the reaction passing through a stage in which a halochromic salt is formed. The major importance of the sulfuric acid in the condensation reaction is that it forms the halochromic salt (II) with aryl amides, the salt acting as an active complex. The fact that the anilide of 2,2',4,4'-tetramethoxydiphenylglycolic acid (VII) can be condensed with a 10% solution speaks against the direct dehydrating action of the sulfuric acid the high dilution excluding the possibility of its dehydrating action: (See top of next page) Moreover, in many cases the sulfuric acid may be replaced by phosphoric and hydrochloric acids, which can likewise form halochromic salts [1].

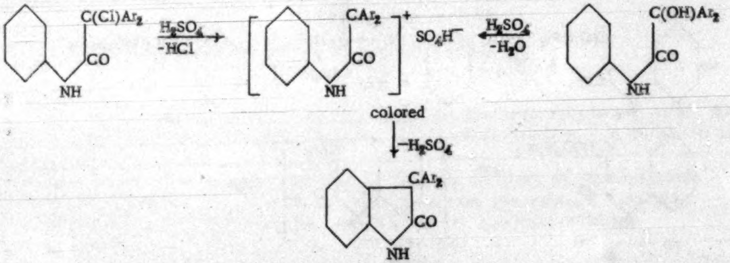
The accelerating action of a rise in temperature and the retarding action of an excess of sulfuric acid upon the condensation rate [2] may be explained on the assumption that the intramolecular dissociation is preceded by dissociation of the ester [I] in accordance with Equation (2). As the temperature is raised, the equilibrium is shifted to the right, and the reaction rate is increased. Increasing the percentage of sulfuric acid suppresses dissociation [3], shifts the equilibrium to the left, and lowers the rate of condensation. Such an explanation fully accords with our experimental findings

The hypothesis that condensation necessarily involves a stage in which a halochromic salt is formed



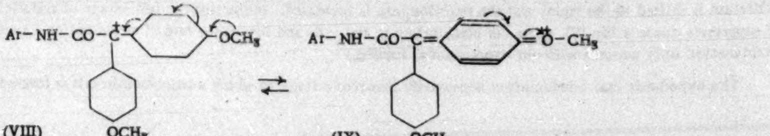
(VII)

was also confirmed in the reaction of the anilide and the β-naphthalide of diphenylchloroacetic acid with concentrated sulfuric acid. The structure of the resulting compounds was established by means of the following schema:



These examples established the ability of the aryl amides of diphenylchloroacetic acid to enter into intramolecular condensations, yielding oxindole derivatives. The intramolecular condensation may, therefore, be regarded as a function of the dissociation of the ester of sulfuric acid and the aryl amide. The significance of a coordination compound that can be dissociated in a Friedel-Crafts reaction has recently been demonstrated in a series of thorough investigations by V. V. Korshak and his associates [4,5].

The aryl amides are condensed within the organic complex ion, so that this condensation may be called an intracomplex reaction. One of the features of this reaction is its high velocity and the high yields of the reaction products. As an intramolecular reaction it will be governed by the internal structure of the organic complex ion. In the present case it is the structure of the cation with a missing electron (a positive charge) at the carbinol carbon atom (III) that is important. The substituents in the radical attached to the nitrogen atom are not linked by a conjugated chain to the central carbon atom and cannot exert any appreciable influence upon the condensation. The substituents in the phenyl radicals attached to the carbinol carbon atom will exert a strong influence. For example, when methyl groups are introduced at the para position, the last π-electrons of the benzene ring will be shifted toward the central carbon atom owing to the +I effects, resulting in a substantial decrease of the rate of condensation [6]. Groups possessing a conjugation effect will exert an even greater influence. In the carbonium ion (VIII) the positive charge is shifted to the oxygen atom (IX) as the result of conjugation in the participation of the oxygen atom of the methoxy group. But since it is (VIII) and not (IX), that enters into the reaction, the condensation rate of such aryl amides will be negligible.



(VIII) (IX)

A negative charge is produced at the ortho position of the aryl amide residue (IV), due to the shift of the unshared electron pair of the nitrogen atom in the direction indicated by the arrows in (III). The charge penetrates into the electron gap of the central carbon atom, an unstable intermediate product (V) being formed, which is stabilized as the result of the evolution of a proton and the formation of the heterocyclic atom (VI). The proton combines with the SO_3H^- to form sulfuric acid (Equation 4), which re-enters the outlined circulatory process.

The mechanism proposed by us for the intramolecular condensation of aryl amides of hydroxy carboxylic acids quite satisfactorily explains the various phases of the reaction, and makes it possible to fix the limits within which the method is usable and to predict the condensation reaction.

EXPERIMENTAL

Anilide of 2,2',4,4'-tetramethoxydiphenylglycolic acid. Initial substances: 6 g (1 mole) of ethyl oxanilate, 43.5 g (5 moles) of the dimethyl ether of 4-iodoresorcinol [1]) and 4 g of magnesium. When the reaction was over, the contents of the flask were decomposed with a saturated solution of ammonium chloride, and the anilide extracted with ether. The yield of the anilide was a few per cent. The bulk of the mass did not decompose, constituting an intermediate reaction product; we had already described the formation of such products [7]. The intermediate product was treated with a 10% solution of sulfuric acid, washed with water until its reaction with Congo red was neutral, dried in the air, and then re-reacted with the organomagnesium compound. With this as our objective, we took 22.5 g of the dimethyl ether of 4-iodoresorcinol and 2.05 g of magnesium. The aggregate yield of the anilide was 1.3 g, or 18% of the theoretical. The anilide crystallized from alcohol as colorless lamellae with an m.p. of 150.5°. It dissolved in concentrated sulfuric acid, producing a blue solution. It constituted colored solutions with 0.1N solutions of sulfuric and hydrochloric acids. The colored solutions were fairly stable and were decolorized only upon heating.

A solution in acetic acid was pale yellow at ordinary temperature, but it turned red at the boiling point of the solvent. This was repeatable a large number of times. This phenomenon in chemistry is called "thermochromism" and is still without a satisfactory explanation [9].

0.2210 g substance: 6.9 ml N_2 (19°, 756 mm). 0.2001 g substance: 6 ml N_2 (19°, 756 mm).
Found %: N 3.59, 3.44. $C_{24}H_{25}O_6N$. Calculated %: N 3.28.

3,3-Bis-(2,4-dimethoxyphenyl)-oxindole. 1 ml of a 10% solution of sulfuric acid was added to a solution of 0.6 g of the anilide of 2,2',4,4'-tetramethoxydiphenylglycolic acid in 7 ml of glacial acetic acid. The red coloring of the solution gradually vanished when the reaction mass was heated on a water bath (60-70°). The substance was insoluble in water or petroleum ether, though freely soluble in other organic solvents. It crystallized when its benzene solution was diluted with petroleum ether. The substance volatilized readily when heated, and was also volatile with steam. M. p. 115° (in a sealed capillary). The yield was 0.35 g, or 61.4% of the theoretical.

0.3302 g substance: 10 ml N_2 (20°, 750 mm). 0.2501 g substance: 7.8 ml N_2 (20°, 750 mm).
Found %: N 3.49, 3.59. $C_{24}H_{23}O_5N$. Calculated %: N 3.46.

3,3-Diphenyloxindole. 3 ml of concentrated sulfuric acid was added to a solution of 0.7 g of the anilide of diphenyl chloroacetic acid in 10 ml of glacial acetic acid. The reaction mass was heated on a water bath (60°) 5-10 minutes until the red coloring disappeared and most of the hydrogen chloride had been eliminated. This yielded 0.6 g, or 96.7% of the theoretical. Crystallization from benzene yielded colorless prisms with an m.p. of 225°. The mixed melting point with a known sample of 3,3-diphenyloxindole exhibited no depression.

3,3-Diphenyl-4,5-benzooxindole (3,3-diphenyl-β-naphthoxindole). Initial substances: a solution of 0.5 g of the β-naphthalide of diphenylchloroacetic acid in 5 ml of glacial acetic acid and 4 g of concentrated sulfuric acid. This yielded 0.43 g, or approximately 100% of the theoretical. Colorless octahedra (from alcohol) with an m.p. of 266°. The mixed melting point with a known sample of 3,3-diphenyl-β-naphthoxindol exhibited no depression.

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[1]) The dimethyl ether of 4-iodoresorcinol was prepared by the Kaufmann and Kieser method [8] and had a b.p. of 162-163° (14 mm).

SUMMARY

1. The mechanism involved in the intramolecular condensation of the N-aryl amides of hydroxy carboxylic acids is proposed and experimentally confirmed.

2. The anilide and the β-naphthalide of diphenylchloroacetic acid are used as examples to establish the ability of the aryl amides of this acid to enter into intramolecular condensation, giving rise to derivatives of oxindole.

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Received February 19, 1950.

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* See Consultants Bureau translation, p. 359.
** Ditto p. 1877.
*** " p. 2343.
**** " p. 2063.
***** " p. 1871.

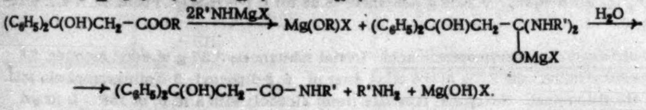
THE N-ARYL AMIDES OF HYDROXY CARBOXYLIC ACIDS AND THEIR CONVERSION INTO HETEROCYCLIC COMPOUNDS

XVI. THE SYNTHESIS OF ARYL AMIDES OF β,β-DIPHENYL-β-HYDROXYPROPIONIC ACID

P. A. Petyunin and A. S. Pesis

The aryl amides of β-hydroxy carboxylic acids are compounds on which only little research has been done, only the acyl derivatives of some aryl amides of β-hydroxy carboxylic acids having been described in the literature [1]. As the result of reacting aryl oxamic and succinanilic acids with organomagnesium compounds, one of the present authors and N. G. Panferova [2,3] have developed preparative methods of synthesizing α- and γ-hydroxy carboxylic acids. An attempt to employ that reaction to synthesize the aryl amides of β-hydroxy carboxylic acids met with failure, since the malonanilic ester reacts with organomagnesium compounds in the enolic form and is recovered unchanged after the reaction mass has been decomposed. Nor did the direct reaction of the ethyl ester of β,β-diphenyl-β-hydroxypropionic acid with aromatic amines yield the desired result.

We went into the reaction of aryl halogen magnesylamines with esters in some detail in order to work out a preparative method for synthesizing the aryl amides of β-hydroxy carboxylic acids, described by Bodraux [4] in his synthesis of the aryl amides of carboxylic and phenolcarboxylic acids. Our experiments have shown that this reaction can be utilized for these purposes, yielding fully satisfactory results. We reacted the ethyl ester of β,β-diphenyl-β-hydroxypropionic acid and RNHMgX, where R = C_6H_5, o-$CH_3C_6H_4$, p-$CH_3C_6H_4$, p-$CH_3OC_6H_4$, p-$C_2H_5OC_6H_4$, α-$C_{10}H_7$ and β-$C_{10}H_7$. The reaction is as follows:



$$(C_6H_5)_2C(OH)CH_2-COOR \xrightarrow{2R'NHMgX} Mg(OR)X + (C_6H_5)_2C(OH)CH_2-\underset{\displaystyle OMgX}{C}(NHR')_2 \xrightarrow{H_2O}$$

$$\longrightarrow (C_6H_5)_2C(OH)CH_2-CO-NHR' + R'NH_2 + Mg(OH)X.$$

The properties of the synthesized aryl amides of β,β-diphenyl-β-hydroxypropionic acid are given in the table.

No.	Formula of aryl amide	M.p.
1	$(C_6H_5)_2C(OH)CH_2CONHC_6H_5$..........	166.5°
2	$(C_6H_5)_2C(OH)CH_2CONHC_6H_4CH_3$-p...	155-156
3	$(C_6H_5)_2C(OH)CH_2CONHC_6H_4CH_3$-o...	167
4	$(C_6H_5)_2C(OH)CH_2CONHC_6H_4OCH_3$-p..	160
5	$(C_6H_5)_2C(OH)CH_2CONHC_6H_4OC_2H_5$-p.	166
6	$(C_6H_5)_2C(OH)CH_2CONHC_{10}H_7$-α.......	186
7	$(C_6H_5)_2C(OH)CH_2CONHC_{10}H_7$-β.......	188.5

EXPERIMENTAL

Anilide of β,β-diphenyl-β-hydroxypropionic acid. A solution of 9.8 g (3 moles) of freshly distilled aniline in 30 ml of ether was added to bromomethylmagnesium, prepared from 13 g (3 moles of ethyl bromide and 2.88 g of magnesium in 30 ml of ether. A solution of 10.8 g (1 mole) of the ethyl ester of β,β-diphenyl-β-hydroxypropionic acid* in 30 ml of ether was added to the resulting suspension or solution of phenylbromomagnesylamine. Finally, the contents of the flask were boiled on a water bath for 1.5-2 hours. After the reaction mass had been decomposed with dilute hydrochloric acid, the precipitate was filtered out, washed on the filter with water until its acid reaction with Congo red had disappeared, and air-dried. Driving off the ether yielded some more of the substance. The anilide was insoluble in water, slightly soluble in ether, and freely soluble in acetone and chloroform. When reacted with conc.sulfuric acid it turns the acid yellow, the color gradually changing to green. Crystallization from alcohol yielded colorless needles with a m.p. of 166.5°. The yield was 6 g, or 47.3% of the theoretical.

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* The ethyl ester of β,β-diphenyl-β-hydroxypropionic acid was prepared by a S.N.Reformatsky reaction [5]; its yield was 60% of the theoretical and its m.p. 84° [6].

0.1500 g substance: 0.4380 g CO_2; 0.0809 g H_2O. 0.1232 g substance: 0.3587 g CO_2; 0.0660 g H_2O. 0.2000 g substance: 6.1 ml 0.1 N H_2SO_4. 0.2270 g substance: 6.88 ml 0.1 N H_2SO_4. Found %: C 79.68, 79.46; H 6.04, 5.99; N 4.27, 4.22. $C_{21}H_{19}O_2N$. Calculated %: C 79.46; H 6.04; N 4.41.

Aniside of β,β-diphenyl-β-hydropropionic acid. Initial substances: 13 g of ethyl bromide, 2.88 g of magnesium, 14.7 g of p-anisidine, and 8.1 g of the ethyl ester of β,β-diphenyl-β-hydroxypropionic acid. This yielded 6 g of the substance, or 58% of the theoretical. Crystallization from alcohol yielded rectangular lamellae with a m.p. of 160°. It colored conc. sulfuric acid dark-yellow, changing to green.

0.2820 g substance: 8.54 ml 0.1 N H_2SO_4. 0.2090 g substance: 6.18 ml 0.1 N H_2SO_4. Found %: N 4.24, 4.14. $C_{22}H_{21}O_3N$. Calculated %: N 4.03.

p-Toluide of β,β-diphenyl-β-hydroxypropionic acid. We took 6.54 g of ethyl bromide, 1.46 g of magnesium, 6.4 g of p-toluidine, and 5.4 g of the ethyl ester of β,β-diphenyl-β-hydroxypropionic acid. The yield was 4 g, or 60% of the theoretical. Crystallization from alcohol yielded needles with a m.p. of 155-156°. It dissolved in conc. sulfuric acid, turning the solution bright-yellow, changing to green.

0.2000 g substance: 6.08 ml 0.1 N H_2SO_4. 0.2123 g substance: 6.44 ml 0.1 N H_2SO_4. Found %: N 4.25, 4.24. $C_{22}H_{21}O_2N$. Calculated %: N 4.23.

o-Toluide of β,β-diphenyl-β-hydroxypropionic acid. The reaction involved 13 g of ethyl bromide, 2.8 g of magnesium, 13 g of o-toluidine, and 8.1 g of the ethyl ester of β,β-diphenyl-β-hydroxypropionic acid. The yield was 6 g, or 62.2% of the theoretical. Colorless needles (from alcohol) with a m.p. of 167°. Solutions in conc. sulfuric acid were yellow, the color turning to green upon standing.

0.1548 g substance: 4.85 ml 0.1 N H_2SO_4. 0.1730 g substance: 5.2 ml 0.1 N H_2SO_4. Found %: N 4.38, 4.23. $C_{22}H_{21}O_2N$. Calculated %: N 4.23.

o-Phenetide of β,β-diphenyl-β-hydroxypropionic acid. Initial substances: 8.7 g of ethyl bromide, 1.9 g of magnesium, 10.9 g of p-phenetidine, and 5.4 g of the ethyl ester of β,β-diphenyl-β-hydroxypropionic acid. The yield was 3.7 g of the substance, or 55% of the theoretical. Colorless needles gathered into clusters (from alcohol) with a m.p. of 166°. The substance dissolved in conc. sulfuric acid, turning it yellow, the color changing to green.

0.2040 g substance: 6.09 ml 0.1 N H_2SO_4. 0.2070 g substance: 6.08 ml 0.1 N H_2SO_4. Found %: N 4.1, 4.11. $C_{23}H_{23}O_3N$. Calculated %: N 3.88.

α-Naphthalide of β,β-diphenyl-β-hydroxypropionic acid. Initial substances: 3.27 g of ethyl bromide, 0.8 g of magnesium, 4.3 g of α-naphthylamine, and 2.7 g of the ethyl ester of β,β-diphenyl-β-hydroxypropionic acid. The yield was 1.5 g, or 40% of the theoretical. Hexagonal lamellae (from alcohol) with a m.p. of 186°. It turned conc. sulfuric acid yellow, the color changing to green.

0,1654 g substance: 4.7 ml 0.1 N H_2SO_4. 0.1800 g substance: 5.35 ml 0.1 N H_2SO_4. Found %: N 3.96, 4.1. $C_{25}H_{21}O_2N$. Calculated %: N 3.8.

β-Naphthalide of β,β-diphenyl-β-hydroxypropionic acid. We took 3.3 g of ethyl bromide, 0.8 g of magnesium, 4.3 g of β-naphthylamine, and 2.3 g of the ethyl ester of β,β-diphenyl-β-hydroxypropionic acid for the reaction. The yield was 1.55 g, or 40% of the theoretical. Colorless needles (from alcohol) with a m.p. of 188.5°. It turned conc. sulfuric acid yellow, the color changing to an emerald-green.

0.1912 g substance: 5.18 ml 0.1 N H_2SO_4. 0.1900 g substance: 5 ml 0.1 N H_2SO_4. Found %: N 3.79, 3.67. $C_{25}H_{21}O_2N$. Calculated %: N 3.8.

SUMMARY

1. The reaction of aryl halogen magnesylamines with the ethyl ester of β,β-diphenyl-β-hydroxypropionic acid has been utilized to develop a preparative method for synthesizing the aryl amides of β-hydroxy carboxylic acids.

2. Several aryl amides of β,β-diphenyl-β-hydroxypropionic acid, not hitherto described in the lierature, have been synthesized and their properties investigated.

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Received October 21, 1950

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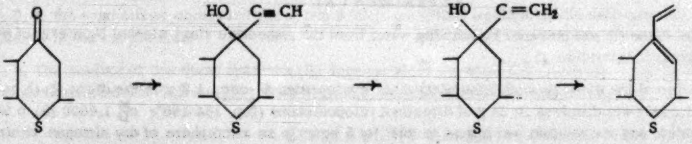
DERIVATIVES OF ACETYLENE

140. HETEROCYCLIC COMPOUNDS

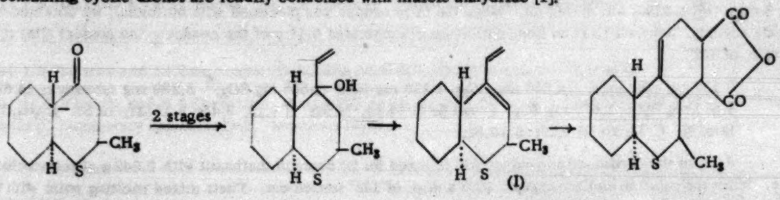
XVI. SYNTHESIS OF SULFUR ANALOGS OF STEROIDS CONTAINING A B THIOPYRAN RING

I.N.Nazarov, I.A.Gurvich, and A.I.Kuznetsova

In our preceding report we described a method for synthesizing sulfur-containing cyclic dienes, based on the tetrahydro-γ-thiopyrones:

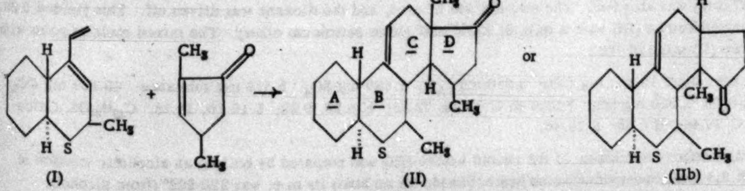


The sulfur-containing cyclic dienes are readily condensed with maleic anhydride [1]:



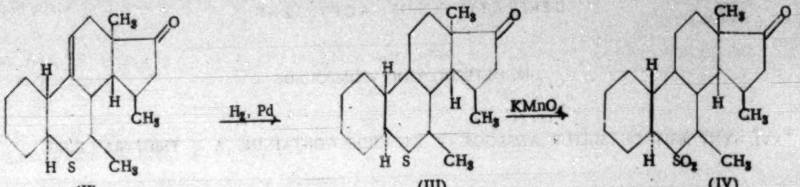
In the present paper we synthesized the sulfur analog of steroids (IIa) or (IIb), in which the B ring is not carboxylic, but a thiopyran ring. Up to now only one product of this kind has been known, which contains sulfur in the D ring and is a derivative of thiopyranophenanthrene [2].

When 2-methyl-4-vinyl-Δ^3-hexahydrothiochromene (I) is heated to 200° for 5 hours with an excess of 1,3-dimethyl-Δ^1-cyclopenten-5-one [3], the crystalline diene condensation product (IIa) or (IIb) is formed, its yield being approximately 12%:



The compound (IIa) or (IIb) has the skeleton of thiochromanoindanone and constitutes the sulfur analog of steroids that contain the B pyran ring. In this compound the A and B rings are connected together in the trans position, since the diene (I) was synthesized from trans-2-methylhexahydrothiochromanone. In conformity with the rule of cis addition during a diene synthesis, the C and D rings in the synthesized compound (IIa) or (IIb) must be linked together in the cis position.

When we hydrogenated the steroid ketone (II) with a Pd catalyst in dioxane, we obtained the saturated compound (III), its oxidation with potassium permanganate yielding the sulfone (IV):



(II) (III) (IV)

It is worthy of note that the unsaturated condensation product (II) does not form a semicarbazone of 2,4-dinitrophenylhydrazone even when heated for a long time with the respective reagents, whereas the hydrogenated compounds (III) and (IV) form 2,4-dinitrophenylhydrazones fairly readily.

EXPERIMENTAL

The initial diene (I) was prepared by splitting water from the respective vinyl alcohol by means of p-toluenesulfonic acid or potassium bisulfate [1].

Condensation of the diene (I) with 1,3-dimethyl-Δ^1-cyclopenten-5-one. 1.8 g of the diene (I) (b.p. 128-129° at 11 mm; n_D^{20} 1.5430) was dissolved in 33 g of dimethylcyclopentenone (b.p. 164-166°; n_D^{20} 1.4600 [3], 0.04 g of pyrogallol was added, and the solution was heated to 200° for 5 hours in an atmosphere of dry nitrogen within a steel ampoule. The dimethylcyclopentenone was driven off in vacuo, after which 0.8 g of the initial diene (b.p. 110-120° at 8 mm; n_D^{20} 1.5290) was driven off. When the tarry residue was processed with methanol, we obtained 0.25 g of crude crystals. Recrystallization from petroleum ether yielded 0.11 g of the condensation product (IIa) or (IIb) with a m.p. of 142°.

5.130 mg substance: 14.060 mg CO_2; 4.210 mg H_2O; 1.585 mg SO_4.[*] 5.290 mg substance: 14.520 mg CO_2; 4.470 mg H_2O; 1.670 mg SO_4. Found %: C 74.80, 74.91; H 9.18, 9.45; S 10.31, 10.53. $C_{19}H_{28}OS$. Calculated %: C 74.95; H 9.27; S 10.52.

0.1 g of the condensation product was refluxed for 20 hours in methanol with 0.042 g of semicarbazide acetate. When the solution cooled, crystals with a m.p. of 142° settled out. Their mixed melting point with the initial substance exhibited no depression.

A hydrochloric acid solution of 0.11 g of the condensation product, 0.07 g of 2,4-dinitrophenylhydrazone, and 0.07 g of hydrochloric acid was boiled for 5 hours, the condensation product again being recovered unchanged.

Hydrogenation of the steroid ketone (II). 0.29 g of the condensation product (II) (b.p. 142°) was hydrogenated with 0.3 g of a Pd catalyst (PdO on $CaCO_3$) in a solution of 18 ml of absolute dioxane. 16 ml of hydrogen was absorbed in 7 hours after which hydrogenation ceased. Another 0.3 g of the Pd catalyst was added, and hydrogenation was continued at 100°. Another 9 ml of hydrogen was absorbed, after which hydrogenation ceased. A total of 25 ml of hydrogen (25°, 737 mm) was absorbed. The solution was filtered, and the dioxane was driven off. This yielded 0.23 g of a saturated steroid ketone (III) with a m.p. of 135.5-136° (from petroleum ether). The mixed melting point with the initial substance (II) was 116-128°.

4.891 mg substance: 13.160 mg CO_2; 3.930 mg H_2O; 1.480 mg SO_4. 5.110 mg substance: 13.660 mg CO_2; 4.210 mg H_2O; 1.550 mg SO_4. Found %: C 73.43, 72.95; H 8.99, 9.22; S 10.10, 10.13. $C_{19}H_{30}OS$. Calculated %: C 74.44; H 9.86; S 10.46.

The 2,4-dinitrophenylhydrazone of the steroid ketone (III) was prepared by boiling an alcoholic solution of the substance with 2,4-dinitrophenylhydrazine hydrochloride for an hour; its m.p. was 220-222° (from alcohol).

2.350 mg substance: 0.254 ml N_2 (23°, 752 mm). Found %: N 12.33. $C_{25}H_{34}O_4N_4S$. Calculated %: N 11.51.

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[*] The substance was simultaneously analyzed for C, H, and S by the Korshun and Shevelova method [4].

Oxidizing the steroid ketone (III). 0.15 g of the substance (III) was dissolved in 10 ml of acetone and 0.38 ml of 10% sulfuric acid was added to the solution, which was then cooled with ice water and agitated while 0.1 g of potassium permanganate was added. The precipitated manganese dioxide was filtered out and washed with acetone. After the acetone had been driven off, the residue was found to consist of crystals of the sulfone (IV), whose m.p. was 186-186.5° (from alcohol).

4.550 mg substance: 11.270 mg CO_2; 3.450 mg H_2O; 1.250 mg SO_4. 4.010 mg substance: 9.910 mg CO_2; 3.100 mg H_2O; 1.150 mg SO_4. Found %: C 67.60; 67.44; H 8.48, 8.65; S 9.17, 9.57. $C_{19}H_{30}O_3S$. Calculated %: C 67.41; H 8.93; S 9.47.

The 2,4-dinitrophenylhydrazone of the sulfone (IV) was partially formed when an alcoholic solution of the sulfone (IV) was reacted with 2,4-dinitrophenylhydrazine hydrochloride in the cold. When an alcoholic solution of 35 mg of the sulfone (IV) and 24 mg of 2,4-dinitrophenylhydrazine was heated, we obtained the 2,4-dinitrophenylhydrazone with a m.p. of 265-266° (from a mixture of benzene and petroleum ether).

SUMMARY

1. A diene condensation has been employed in synthesizing for the first time the sulfur analogs of the steroid (IIa) or (IIb), which contain sulfur in the ring B.

2. In the synthesized compound the A and B rings are linked together in the trans position, the rings C and D being linked in the cis position.

3. The product of the diene synthesis (II) does not yield the usual derivatives at the carbonyl group, though the hydrogenated products (III) and (IV) readily yield 2,4-dinitrophenylhydrazones.

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Received July 29, 1950

Institute of Organic Chemistry,
USSR Academy of Sciences

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*See Consultants Bureau translation, p. a-637.

DERIVATIVES OF ACETYLENE

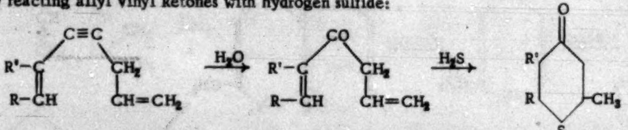
141. HETEROCYCLIC COMPOUNDS

XVII. THE STRUCTURE OF TETRAHYDRO-γ-THIOPYRONES AND THE MECHANISM OF THEIR FORMATION.

KIZHNER REDUCTION OF TETRAHYDRO-γ-THIOPYRONES

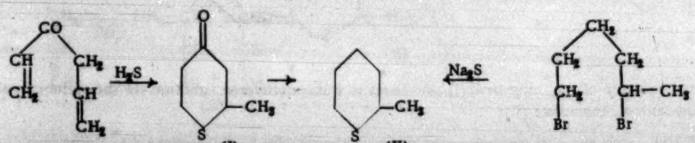
I.N. Nazarov, I.A. Gurvich, and A.I. Kuznetsova

In one of our preceding reports we described a new and simple method of synthesizing various tetrahydro-γ-thiopyrones by reacting allyl vinyl ketones with hydrogen sulfide:



R and R' = hydrogen or an alkyl group

We decided to reduce 2-methyltetrahydro-1-thiopyran-4-one (I) to the known α-methylpentamethylene sulfide (II), obtained by a Grishkevich-Trokhimovsky reaction of sodium sulfide with 1,5-dibromohexane, about whose six-membered ring structure there is no doubt [2], in order to establish the structure of the tetrahydro-γ-thiopyrones we had synthesized:



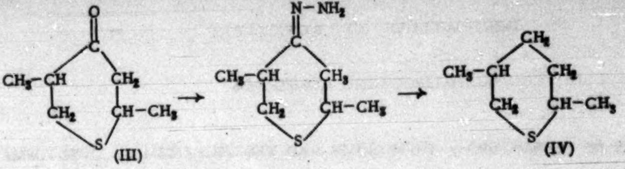
(I) (II)

The Clemmensen method has been employed in most of the known instances of the reduction of tetrahydro-γ-thiopyrones to tetrahydrothiopyrans. This was the method used to reduce 2,6-diphenyltetrahydro-1,4-thiopyrone [3], 2,2,6,6-tetramethyltetrahydro-1,4-thiopyrone [4], as well as several thiochromanones [5], thiophene ketones [6], and homothiochromanone [7] to the respective thiopyrans.

Instances are also known, however, of the reduction of aldehydes and ketones of the thiophene [8] and thioxanthone [9] series by the Kizhner method. This method has also been utilized in reducing the dimer of acrolein, which is an aldehyde of the pyran series [10]. We tried to reduce 2-methyltetrahydro-1-thiopyran-4-one (I) by the Clemmensen method, using alcohol as the solvent, but the main result we secured was rupture of the ring.

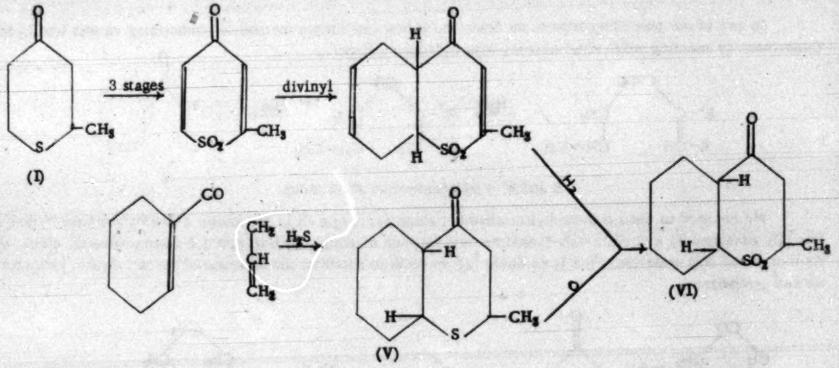
Then we resorted to the Kizhner method to reduce the tetrahydro-γ-thiopyrones. The reaction was carried out in ethylene glycol without precipitating a hydrazone. Reducing 2-methyltetrahydro-1-thiopyran-4-one (I) by the Kizhner method yielded 2-methyltetrahydrothiopyran (II), the yield being 62%. The constants of the synthesized thiopyran (II), the melting point of the corresponding sulfone, and the sublimation point of its methiodide, all agreed with the constants for α-methylpentamethylene sulfide given in the literature [2]. We have therefore shown that the cyclic sulfur-containing ketone synthesized by reacting allyl vinyl ketone with hydrogen sulfide actually has a six-membered ring structure.

When we reduced 2,5-dimethyltetrahydro-1-thiopyran-4-one (III) by the Kizhner method, we secured a 61% yield of 2,5-dimethyltetrahydrothiopyran (IV), oxidation of which with potassium permanganate yielded a liquid sulfone. The crystalline derivatives of the thiopyran (IV) with methyl iodide and mercuric chloride were likewise obtained:



The formation of a six-membered thiopyran ring when allyl vinyl ketones are acted upon by hydrogen sulfide has also been demonstrated in bicyclic systems.

The product of the diene condensation of 2-methylthiopyrone dioxide with butadiene yields the sulfone (VI) upon reduction in an acid medium; this sulfone was previously obtained by reacting hydrogen sulfide with allyl Δ^1-cyclohexenyl ketone, followed by oxidizing the resultant thiochromanone (V):

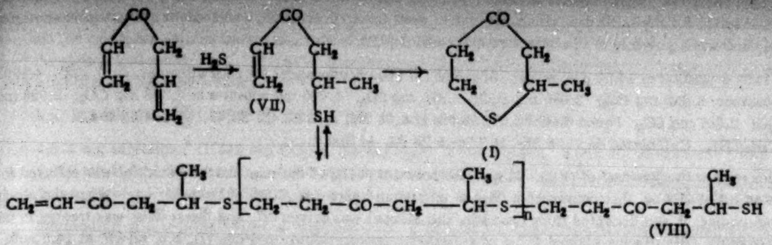


The six-membered structure of the thiopyrone (I) thus leads to a six-membered structure for the sulfur-containing ring of the hexahydrothiochromanone (V).

These findings, together with the conversion of several tetrahydro-γ-thiopyrones into thiopyrone dioxides that we have carried out recently and the behavior of the latter in a diene synthesis incontrovertibly prove the six-membered structure of the sulfur-containing heterocyclic compounds we have synthesized by adding hydrogen sulfide to allyl vinyl ketones and divinyl ketones.

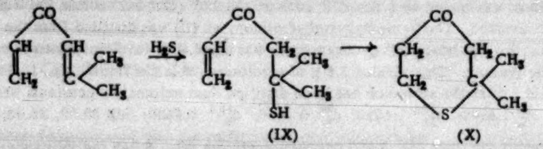
As we had established previously [1], the yield of tetrahydro-γ-thiopyrones is as high as 70% when allyl vinyl ketones are reacted with hydrogen sulfide. The yield of 2-methyltetrahydro-1-thiopyran-4-one (I) was only 30%, however. The reason for so low a yield in this instance was the formation of large quantities of a polymer of the unsaturated ketone (VII). We found that formation of the polymer promoted an interruption of the reaction between the stage in which the ketothiol was formed and that in which it was cyclized. By effecting cyclization as soon as the ketothiol had been synthesized we secured a 65% yield of the 2-methyltetrahydrothiopyrone (I).

Analysis of the polymer indicated that it was the trimer of the unsaturated ketothiol (VII). The polymer exhibited the qualitative reactions for the sulfhydryl group with nitrous acid and sodium nitroprusside. When the polymer (VIII) was boiled with a dilute solution of an alcoholic alkali, it was partially cleaved, yielding the ketothiol (VII) and then cyclizing it to the thiopyrone (I), which we found in the reaction products. We had previously observed this sort of cleavage of a sulfide when it was boiled in dilute alcoholic solutions of an alkali [11]: it pointed to the presence of sulfide bonds in the polymer (VIII). Our results enable us to picture the reaction involved in the formation of 2-methyltetrahydro-1-thiopyran-4-one as follows:

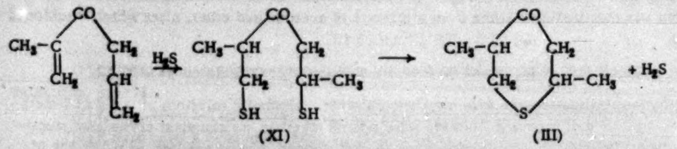


The first stage of the addition of hydrogen sulfide to an allyl vinyl ketone is the formation of the unsaturated ketothiol (VII), which is readily cyclized to 2-methyltetrahydro-1-thiopyran-4-one (I) by heating it with sodium acetate and is polymerized in the cold to the product (VIII).

As Nazarov and Kuznetsova had shown previously [12], β,β-dimethyl divinyl ketone behaves similarly in a reaction with hydrogen sulfide. This yields an unsaturated ketothiol (IX), which is cyclized to 2,2-dimethyltetrahydro-1,4-thiopyrone (X) when heated with sodium acetate and is converted to the corresponding polymer when stored.



This is not the only possible way of producing tetrahydro-γ-thiopyrones from unsaturated ketones, however. As we know, allyl isopropenyl ketone can add two molecules of hydrogen sulfide under these conditions, the resultant ketodithiol (XI) being stable in the cold, though it is readily cyclized when heated in an alkaline medium, giving off hydrogen sulfide:



2-Methyltetrahydro-1-thiopyran-4-one (I). a) 10 g of anhydrous sodium acetate was dissolved in 200 ml of 96% alcohol, the flask was immersed in ice water, and hydrogen sulfide was passed through the solution for 30 minutes. Then 12 g of vinyl allyl ketone (b.p. 60-62° at 28 mm; n_D^{20} 1.4690) [13] was added to the solution in the course of 20 minutes, with continuous stirring and the hydrogen sulfide passing through the solution continuously [13]. Hydrogen sulfide was passed through for 30 more minutes after the vinyl allyl ketone had been added, and then the solution was refluxed for 5 hours. The mercaptan odor disappeared. The alcohol was driven off on a water bath, 30 ml of water was added, and the product was extracted with ether, washed with water, dried with sodium sulfate, and distilled in vacuo. This yielded 10.5 g of the previously described [1] 2-methyltetrahydro-1-thiopyran-4-one (I), with a b.p. of 84-85° at 13 mm, n_D^{20} 1.5090, representing 65% of the theoretical yield.

b) 6 g of anhydrous sodium acetate was dissolved in 200 ml of alcohol, and the solution was saturated with hydrogen sulfide at 0°. The solution was continuously stirred for one hour with uninterrupted passage of the hydrogen sulfide while 25.5 g of vinyl allyl ketone was added. Then hydrogen sulfide was passed through for another 4 hours, and the solution was allowed to stand overnight. A transparent, viscous layer of resin formed on the bottom of the flask. Another 200 ml of alcohol and 4 g of sodium acetate were added, and the solution was boiled for 8 hours. After the solution had cooled, it was decanted from the resin and processed as described in the preceding experiment. This yielded 5.4 g of 2-methyltetrahydrothiopyrone (I), b.p. 70.5-72° at 8.5 mm; n_D^{19} 1.5094. 12 g of a polymerized residue, which decomposed when heated, was left in the distilling flask. The transparent resin secured after the solution had been boiled was washed with water and acetone, filtered, and dried over phosphoric anhydride in a vacuum desiccator. The resultant viscous, transparent resin was sparingly soluble in the usual solvents, exhibited a qualitative reaction for the sulfhydryl group with nitric acid (green coloration) and sodium nitroprusside (crimson coloration), and was a polymer of the unsaturated ketothiol (VII), with triple its molecular weight:

0.1196 g substance: 17.00 g dioxane: Δt 0.082°. 0.1600 g substance: 16.25 g dioxane: Δt 0.112°. 4.220 mg substance: 8.625 mg CO_2; 3.050 mg H_2O; 2.970 mg SO_4. 4.095 mg substance: 8.378 mg CO_2; 2.990 mg H_2O; 2.861 mg SO_4. Found %: C 55.77, 55.83; H 8.08, 8.17; S 23.46, 23.42. M 394.6, 404.3. $(C_6H_{10}OS)_3$. Calculated %: C 55.35; H 7.74; S 24.63. M 390.6.

Cleavage of the polymer of (VII). 4 g of the polymer (VIII) of the unsaturated ketothiol was refluxed for 8 hours with 40 ml of alcohol that contained 0.08 g of potassium hydroxide (0.2% of the solution). When the alcoholic solution had cooled, it was decanted from the resin, the alcohol was driven off, and the residue was treated in the customary manner. Distillation yielded 0.7 g of 2-methyltetrahydrothiopyran-4-one (I), b.p. 88-89° at 14.5 mm; n_D^{23} 1.5060.

2-Methyltetrahydrothiopyran (II). (α-Methylpentamethylene sulfide). 6.5 g of 2-methyltetrahydro-1-thiopyran-4-one (I) (b.p. 59-60° at 6 mm; n_D^{20} 1.5094), 40 ml of ethylene glycol, and 10 ml of hydrazine hydrate were placed in a three-necked round-bottomed flask, fitted with a thermometer immersed in the liquid and a descending condenser. The solution was heated to 130-160°, about 5 ml of a cloudy liquid being driven off. Then the solution was cooled to 40°, and 6 g of fused potassium hydroxide was added. The descending condenser was replaced by a reflux condenser and the flask was heated on a metallic bath at 140-170° (125-142° within the liquid) for 6 hours until no more nitrogen was evolved. The 2-methyltetrahydrothiopyran (II) was distilled from the reaction mixture, and the distillate was extracted with ether. The ether extract was dried with calcium chloride, and the product was fractionated at atmospheric pressure. This yielded 3.6 g of a colorless, volatile liquid, b.p. 150-152.5°, constituting 62% of the theoretical yield. After the substance had been distilled over sodium, its constants were as follows: b.p. 150.5-151.5° at 755 mm; n_D^{20} 1.4902; $n_D^{18.5}$ 1.4910; d_4^{20} 0.9406; $d_4^{18.5}$ 0.9438; MR 35.73, 35.66; calc. 35.68.

5.910 mg substance: 13.435 mg CO_2; 5.527 mg H_2O; 4.870 mg SO_4. 6.348 mg substance: 14.463 mg CO_2; 5.970 mg H_2O; 5.215 mg SO_4. 4.662 mg substance: 10.590 mg CO_2; 4.333 mg H_2O. Found %: C 62.04, 62.17, 61.99; H 10.46, 10.52, 10.40; S 27.50, 27.42. $C_6H_{12}S$. Calculated %: C 62.04; H 10.41; S 27.58.

Methiodide of 2-methyltetrahydrothiopyran. 0.4 g of 2-methyltetrahydrothiopyran (II) and 0.6 g of methyl iodide were poured into a flask with a ground-glass stopper. A week later elongated needles of the methiodide were filtered out. The methiodide was recrystallized twice from a mixture of acetone and ether, after which it sublimed at 158-159° without melting.

3.450 mg substance: 1.335 ml 0.02 N I_2. Found %: S 12.40. $C_6H_{12}S \cdot CH_3I$. Calculated %: S 12.42.

Compound of 2-methyltetrahydrothiopyran with mercuric chloride. Alcoholic solutions of 0.4 g of 2-methyltetrahydrothiopyran (II) and of 0.95 g of mercuric chloride were poured together, an abundant crystalline precipitate being thrown down at once. Double recrystallization from alcohol yielded minute needles, m.p.102-102.5°.

6.030 mg substance: 1.536 ml 0.02 N I_2. 4.390 mg substance: 1.145 ml 0.02 N I_2. Found %: S 8.16, 8.17. $C_6H_{12}S \cdot HgCl_2$. Calculated %: S 8.27.

2-Methyltetrahydrothiopyran dioxide. 1 g of 2-methyltetrahydrothiopyran (II) was dissolved in 60 ml of acetone, and the solution was stirred continuously and water-cooled while 6.1 ml of 10% sulfuric acid and 2.2 g of powdered potassium permanganate were added to it during the course of 30 minutes. Stirring was continued for another hour. Then the manganese dioxide was filtered out and washed several times with acetone. Driving off the solvent in vacuo left a residue of 1 g of a crystalline sulfone. Three recrystallizations from a mixture of ether and petroleum ether yielded elongated needles, m.p. 68-68.5°.

4.212 mg subtance: 7.505 mg CO_2; 3.083 mg H_2O; 2.770 mg SO_4. 5.640 mg substance: 10.042 mg CO_2; 4.133 mg H_2O; 3.650 mg SO_4. Found %: C 48.63, 48.64; H 8.19, 8.20; S 21.95, 21.60. $C_6H_{12}O_2S$. Calculated %: C 48.60; H 8.15; S 21.62.

Data in the literature [2] for α-methylpentamethylene sulfide: b.p. 151.4-151.6° at 750 mm (corr); d_4^{185} 0.9449; $n_D^{18.5}$ 1.4884; subliming point of the methiodide: 158-159°; melting point of the mercuric chloride compound: 97-98°; melting point of α-methylpentamethylene sulfone: 68-68.5°.

2,5-Dimethyltetrahydrothiopyran (IV). 7.2 g of the previously described tetrahydro-1-thiopyran-4-one (III) [1] (m.p. 71°), 40 ml of ethylene glycol, and 10 ml of hydrazine hydrate were heated together to 130-160° as described in the preceding experiment 6 ml of a cloudy liquid being distilled off in the course of 30 minutes. Then the solution was cooled, and 5 g of fused potassium hydroxide was added to it. The reaction mixture was refluxed, nitrogen beginning to evolve when the temperature of the liquid reached 125°. Heating was continued for 5 hours at a solution temperature of 143-147° (bath temperature 162-167°) until no more nitrogen was given off. Then the 2,5-dimethyltetrahydrothiopyran (IV) was distilled from the reaction mixture, the distillate being extracted with ether, and the ether extract dried with calcium chloride. Fractionation yielded 4 g of a volatile colorless liquid, or 61% of the theoretical yield; b.p. 162-164°. The constants of the 2,5-dimethyltetrahydrothiopyran (IV) were as follows after distillation over sodium:

B.p. 163-163.5°; n_D^{20} 1.4850; d_4^{20} 0.9230; MR 40.43; calculated 40.30.

4.872 mg substance: 11.512 mg CO_2; 4.725 mg H_2O; 3.570 mg SO_4. 4.420 mg substance: 10.420 mg CO_2; 4.250 mg H_2O; 3.240 mg SO_4. 4.628 mg substance: 10.947 mg CO_2; 4.500 mg H_2O. Found %: C 64.48, 64.34, 64.55; H 10.84, 10.76, 10.88; S 24.46, 24.47. $C_7H_{14}S$. Calculated %: C 64.59; H 10.83; S 24.62.

Methiodide of 2,5-dimethyltetrahydrothiopyran. 0.34 g of 2,5-dimethyltetrahydrothiopyran and 0.7 g of methyl iodide were poured together in a flask with a ground-glass stopper. After a week had elapsed, the resulting crystals were filtered out and recrystallized from acetone. The methiodide of 2,5-dimethyltetrahydrothiopyran consists of colorless needles that sublime at 141-142°.

3.050 mg substance: 1.157 ml 0.02 N I_2. Found %: S 12.15. $C_7H_{14}S \cdot CH_3I$. Calculated %: S 11.78.

Mercuric chloride compound of 2,5-dimethyltetrahydrothiopyran. Alcoholic solutions of 0.4 g of 2,5-dimethyltetrahydrothiopyran and of 0.95 g of mercuric chloride were poured together. An abundant crystalline precipitate was thrown down at once. Double recrystallization from alcohol yielded minute needles with a m.p. of 121-121.5°.

5.650 mg substance: 1.343 ml 0.02 N I_2. 5.430 mg substance: 1.322 ml 0.02 N I_2. Found %: S 7.61, 7.80. $C_7H_{14}S \cdot HgCl_2$. Calculated %: S 7.98.

SUMMARY

1. It has been demonstrated that the sulfur heterocyclic compounds produced by the action of hydrogen sulfide upon vinyl allyl ketones have a six-membered ring.

2. Kizhner reductions of the tetrahydro-γ-thiopyrones yielded 60% of the respective tetrahydrothiopyrans.

3. The yield of 2-methyltetrahydro-1-thiopyran-4-one (I) has been improved, and a suggestion is made concerning the mechanism involved in its formation.

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Received July 29, 1950

Institute of Organic Chemistry
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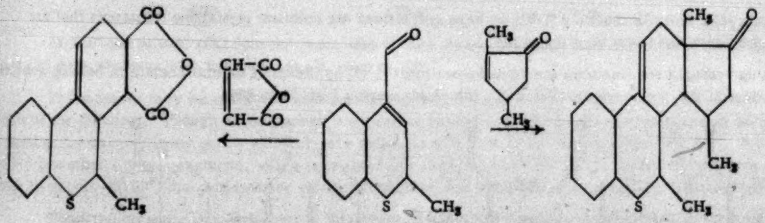
DERIVATIVES OF ACETYLENE

142. HETEROCYCLIC COMPOUNDS

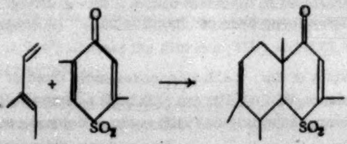
XVIII. DIENE SYNTHESIS BASED UPON DIOXIDES OF DISUBSTITUTION DERIVATIVES OF γ-THIOPYRONES

I.N. Nazarov, I.A. Gurvich, and A.I. Kuznetsova

In our previous researches we started out with tetrahydro-γ-thiopyrones and prepared sulfur-containing cyclic dienes, which were used in diene syntheses to secure polycyclic sulfur compounds [1,2]:

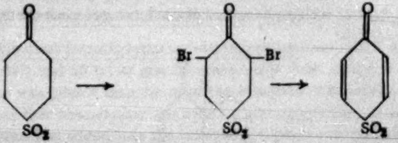


Another possible way of constructing sulfur-containing polycyclic compounds based on tetrahydro-γ-thiopyrones consisted of preparing thiopyrone dioxides and using them as the olefin constituents in a diene synthesis:

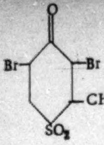


In our present research we have secured several dioxides of substitution derivatives of the γ-thiopyrones and investigated their condensation with butadiene; this yielded compounds with an angular methyl group.

The usual method of preparing dioxides of the γ-thiopyrones involves the bromination of the dioxides of the tetrahydro-γ-thiopyrones, followed by splitting off hydrogen bromide:



This method was used to secure the dioxides of thiopyrone and dihydrothiopyrone [3,4], 2,6-dimethylthiopyrone [5], 2,6-diphenylthiopyrone [6], and of various thiochromones [7]. We used this method to secure several new dioxides of substitution derivatives of γ-thiopyrones from the dioxides of various tetrahydro-γ-thiopyrones previously described by us [8].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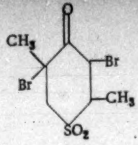
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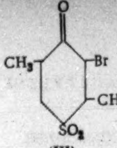
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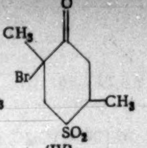
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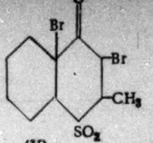
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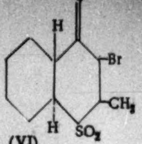
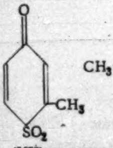

(VI)

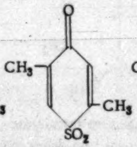
When two molecules of bromine were heated with a solution of 2-methyltetrahydro-1-thiopyran-4-one in glacial acetic acid, we obtained the corresponding cyclic dibromoketosulfone (I), the yield being 86%. A quantitative yield of the cyclic dibromoketosulfone (II) was similarly prepared from the dioxide of 2,5-dimethyltetrahydro-1-thiopyran-4-one. The action of one molecule of bromine upon 2,5-tetrahydro-1-thiopyran-4-one under the same conditions yielded a mixture of the isomeric monobromoketosulfones (III) and (IV), the yield being 88%. When one molecule of bromine was reacted with a solution of 2,5-dimethyltetrahydro-1-thiopyran-4-one at room temperature, with hydrogen bromide present as a catalyst, we secured a mixture of the monobromides (III) and (IV), with a lower yield, though the product that predominated in this latter mixture was the tertiary monobromoketosulfone (IV).

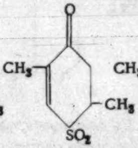
Bromination of the dioxide of trans-2-methylhexahydro-1-thiochroman-4-one with two molecules or one molecule of bromine yielded, respectively, the bicyclic dibromosulfone (V), the yield being 91%, and the monobromosulfone (VI), the yield being 60%, both belonging to the trans series of compounds.

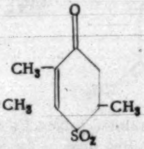
All the cyclic bromoketosulfones (I-VI) we have synthesized are colorless crystalline substances that are stable in the pure state when kept for a long time.

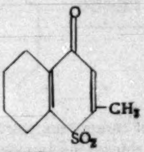
Splitting hydrogen bromine from the bromoketosulfones (I-VI) by means of sodium acetate in boiling acetone produced dioxides of the γ-thiopyrones (VII-XII), the yields ranging from 70 to 80%:

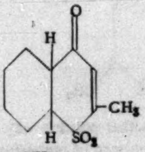

(VII)


(VIII)


(IX)


(X)


(XI)

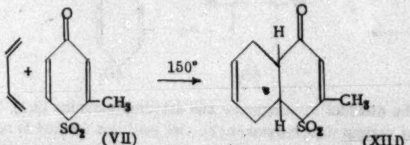

(XII)

The bicyclic sulfone (XII), produced by splitting hydrogen bromide out of the bromosulfone (VI), has a trans configuration.

The properties of the synthesized dioxides of the γ-thiopyrones resemble those of the 1,4-benzoquinones. The sulfones (VII-X) cause sneezing. The sulfones (VII), (VIII), and (XI) have a lemon-yellow color. The sulfones (VII) and (VIII) stain the skin yellow. The oxime of the sulfone (VIII) is also a colored compound.

We know that unsaturated α,β-sulfones enter into condensation with 1,3-dienes like the unsaturated α,β-ketones [9].

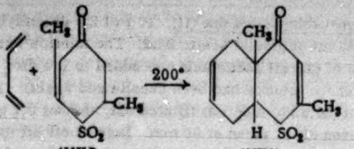
The dioxide of 1,4-thiopyrone [4] reacts with butadiene extremely readily, resembling quinone in this respect. The dioxides of the substituted γ-thiopyrones we synthesized (VII-IX) likewise condense readily with butadiene, though the temperatures required are higher. When the sulfone (VII) is dissolved in dioxane and heated to 150° for 4-5 hours in a steel ampoule together with an excess of divinyl, we get cis-2-methyl-5,8,9,10-tetrahydro-1-thiochromen-4-one (XIII), the yield being 92%:


(VII)

(XIII)

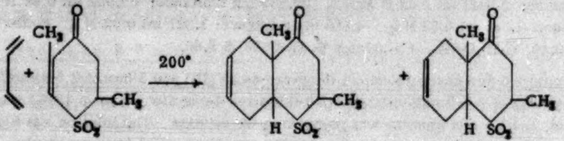
Raising the temperature to 200° does not affect this result: the condensation products exhibit no signs of thioxanthone derivatives, which might have been produced by the addition of two molecules of divinyl to the sulfone (VII).

The sulfone (VIII) condenses with butadiene at 200°, producing a yield of 61% of the dioxide of cis-2,10-dimethyl-5,8,9,10-tetrahydro-1-thiochromen-4-one (XIV). At 150° a large part of the initial sulfone (VIII) is recovered from the reaction:



(VIII) (XIV)

The sulfone (IX) also reacts with butadiene at 200°, producing two stereoisomeric dioxides of cis-2,10-dimethyl-5,8,9,10-tetrahydro-1-thiochroman-4-one (XV), the overall yield being 65%:



(IX) (XVa) (XVb)

At 150° the sulfone (IX) does not react with divinyl, being recovered from the reaction unchanged. The sulfone (X) does not react with butadiene at all, even at 200°.

These results may be compared with the findings on the condensation of butadiene with substitution derivatives of the quinones. Though benzoquinone itself can be readily condensed with two molecules of butadiene [10], 2-methyl-1,4-benzoquinone reacts with only one molecule of butadiene at temperatures up to 110°, while in the case of 2,5-dimethyl-1,4-benzoquinone, which does enter into condensation with two molecules of butadiene at temperatures in excess of 100°, the condensation product containing one molecule of butadiene predominates [12].

Thus, the presence of substituents in thiopyrone dioxides hampers their condensation with butadiene, as in the case of the quinones. Our findings indicate that the position of the substituent in the thiopyrone ring is of major importance for the diene condensation. The inability of the sulfone (XIII), or of the similarly constructed sulfone (XIV), to enter into diene synthesis with a second molecule of butadiene is due to the presence of a substituent at the 2 position. This assumption is borne out by the fact that one of the dihydrothiopyrone dioxides (X) also fails to enter into diene synthesis at 200°, whereas the dioxides (VIII) and (IX), which are substituted at the 5 position, react with butadiene readily at 200°.

Hence, the presence of methyl groups at the α-position to the ketone group merely hampers the reaction, while the presence of substituents at the α-position to the sulfone group renders the condensation of thiopyrone dioxides with butadiene impossible, even at 200°.

EXPERIMENTAL

The initial sulfones were prepared by oxidizing tetrahydro-γ-thiopyrones with potassium permanganate in acetone [8].

I. Bromination of Dioxides of Tetrahydro-γ-thiopyrones

Dioxide of 3,5-dibromo-2-methyltetrahydro-1-thiopyran-4-one (I). 4.4 g of 2-methyltetrahydro-1-thiopyran-4-one dioxide (m.p 79-80°) and 50 ml of glacial acetic acid were placed in a three-necked round-bottomed flask, then 4.1 g of bromine was poured into the resulting solution. The solution was heated to 65-67° on a water bath with vigorous stirring. At that temperature the solution was decolorized instantaneously. The bath was taken away, and another 4 g of bromine was added. As the solution cooled, 6 g of the dibromide settled out, while another 1.5 g of the dibromide settled out when part of the acetic acid was driven off in vacuo (30-40 mm). The product totaled 7.5 g, or 86% of the theoretical yield. The dibromoketosulfone (I) consisted of colorless crystals with a m.p. of 219-219.5° (from acetic acid).

2.860 mg substance: 2.355 mg CO_2; 0.610 mg H_2O. 5.911 mg substance: 4.895 mg CO_2; 1.355 mg H_2O; 4.745 mg SO_4 + Br[*]. Found %: C 22.47, 22.60; H 2.38, 2.57; S 10.13; Br 50.26. $C_6H_8O_3SBr_2$. Calculated %: C 22.52; H 2.53; S 10.02; Br 49.94.

Dioxide of 3,5-dibromo-2,5-dimethyltetrahydro-1-thiopyran-4-one (II). 10 g of 2,5-dimethyltetrahydro-1-thiopyran-4-one dioxide (m.p. 138°) was dissolved in 80 ml of glacial acetic acid. The solution was heated to 65° and vigorously stirred while 18 g of bromine in 20 ml of glacial acetic acid was added to it a drop at a time during the course of 2 hours. (Each drop was added only after the solution had been decolorized again). Then the solution was allowed to stand overnight. The next day 12 g of the dibromide was filtered out, another 3.1 g of the dibromide settling out after part of the acetic acid had been driven off in vacuo at 50 mm. Driving off all the solvent yielded another 3.5 g of the dibromide in the residue. Thus the dibromide (II) produced totaled 18.6 g, which was nearly the quantitative yield. The dibromoketosulfone (II) consisted of colorless crystals with a m.p. of 184.5-185° (from acetone).

31.621 mg substance: 0.9411 ml 0.02 N $AgNO_3$. 22.830 mg substance: 0.6802 ml 0.02 N $AgNO_3$. 4.588 mg substance: 1.381 ml 0.02 N I_2. 4.503 mg substance: 1.321 ml 0.02 N I_2. Found %: Br 47.57, 47.62; S 9.64, 9.40. $C_7H_{10}O_3SBr_2$. Calculated %: Br 47.85; S 9.60.

Dioxides of 3-bromo-2,5-dimethyltetrahydro-1-thiopyran-4-one (III) and 5-bromo-2,5-dimethyltetrahydro-1-thiopyran-4-one (IV). a) 6.8 g of 2,5-dimethyltetrahydro-1-thiopyran-4-one dioxide (m.p. 138%) was dissolved in 130 ml of glacial acetic acid, and 6.2 g of bromine was poured into the solution. The solution was vigorously stirred while being heated to 63-65°, at which temperature the solution was decolorized instantaneously. The solution was cooled and set aside to stand overnight. The next day 2.9 g of a crystalline dibromide with a m.p. of about 200° was filtered out of the reaction mass. Then the acetic acid was gradually driven off at a 30-mm vacuum, and another 7.9 g of bromide crystals was collected fractionally. The crystals collected constituted a mixture of the bromides (III) and (IV), which was separated into two fractions by fractional crystallization. The 5 g of crystals in the first fraction fused at about 200°. Two recrystallizations from acetone yielded the bromoketosulfone (III) with a m.p. of 195-200°.

23.410 mg subs.: 0.4588 ml 0.02 N $AgNO_3$. 25.900 mg subs.: 0.5042 ml 0.02 N $AgNO_3$. 3.455 mg subs.: 1.330 ml 0.02 N I_2. 3.970 mg subs.: 1.539 ml 0.02 N I_2. Found %: Br 31.26, 31.09; S 12.34, 12.42. $C_7H_{11}O_3SBr$. Calculated %: Br 31.32; S 12.56.

The second crystal fraction, totaling 4.3 g, fused at 130-135°. Six recrystallizations from acetic acid and alcohol yielded the bromoketosulfone (IV) with a m.p. of 144-145°.

22.876 mg subs.: 0.4392 ml 0.02 N $AgNO_3$. 26.064 mg subs.: 0.5038 ml 0.02 N $AgNO_3$. Found %: Br 30.78, 30.90. $C_7H_{11}O_3SBr$. Calculated %: Br 31.32.

The aggregate yield of the isomeric bromosulfones totaled 10.8 g, representing 88% of the theoretical yield.

b) 8.8 g of 2,5-dimethyltetrahydro-1-thiopyran-4-one dioxide (m.p. 138°) was dissolved in 100 ml of glacial acetic acid, and 1 ml of a 4N solution of hydrogen bromide in glacial acetic acid was added. The solution was vigorously stirred for 2 hours while 7.9 g of bromine in 20 ml of acetic acid was added. Then much of the acetic acid was driven off at a 25-30 mm vacuum. This yielded a mixture of the bromides (III) and (IV), from which 1.5 g of the high-melting bromide (III) with a m.p. of 199-200° was isolated. The residual mass fused at from 100° to 136°, 1.4 g of the low-melting monobromide (IV), with a m.p. of 144-145°, being isolated from it by fractional crystallization from alcohol. In addition, we secured 2.9 g of a fraction with a m.p. of 124-135° plus 2.5 g with a m.p. of 105-110°. When sodium acetate was used to split HBr from the last two fractions (see below), we secured 1.9 g of the sulfone (IX), corresponding to the low-melting monobromide (IV).

Dioxide of 3,5-dibromo-2-methylhexahydro-1-thiochroman-4-one (V). 5 g of 2-methylhexahydro-1-thiochroman-4-one dioxide (m.p. 157-158°) was dissolved in 40 ml of glacial acetic acid, 7.5 g of bromine was added to the solution, and the whole was vigorously stirred while it was heated to 85°. The solution was instantaneously decolorized at that temperature. As the solution cooled, 6.2 g of the dibromide settled out. Another 1.75 g of the dibromide settled out when part of the acetic acid was driven off in vacuo. The total yield was 7.9 g, or 91% of the theoretical. The dibromosulfone (V) consisted of colorless crystals with a m.p. of 186-187° (from alcohol).

8.144 mg subs.: 9.492 mg CO_2; 2.815 mg H_2O; 5.610 mg SO_4 + Br. Found %: C 31.81; H 3.87; S 8.75; Br 43.21. $C_{10}H_{14}O_3SBr_2$. Calculated %: C 32.10; H 3.77; S 8.57; Br 42.72.

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[*] The analysis was performed by the M.O.Korshun method, the percentages of Br and S being found from the total gain in weight [13].

In another test in which the bromine was added portionwise, 17% of the monobromide (VI) was secured in addition to the dibromide (V)

Dioxide of 3-bromo-2-methylhexahydro-1-thiochroman-4-one (VI). 4.3 grams of 2-methylhexahydro-1-thiochroman-4-one dioxide (m.p. 157-158°) was dissolved in 50 ml of glacial acetic acid. and 3.2 g of bromine was added to the solution. The solution was vigorously stirred as it was heated to 74°, at which temperature it was instantaneously decolorized. As the solution cooled, 2.4 g of the monobromide (VI), with an m.p. of approximately 215°, settled out. Another 1.5 g of crystals of the monobromide, with an m.p. of 202°, settled out when part of the acetic acid was driven off in vacuo. The monobromide totaled 3.4 g, representing 60% of the theoretical.

The bromosulfone (VI) consisted of colorless crystals with an m.p. of 215-216° (from alcohol).

4.194 mg substance: 6.210 mg CO_2; 1.895 mg H_2O. 3.370 mg substance: 5.010 mg CO_2; 1.520 mg H_2O; 2.005 mg SO_4 + Br. Found %: C 40.57, 40.56; H 5.06 5.05; S 10.82; Br 26.96. $C_{10}H_{13}O_3SBr$. Calculated %: C 40.57; H 5.12; S 10.86; Br 27.06.

II. Splitting Hydrogen Bromide Out of the Brominated Dioxides of Tetrahydro-γ-thiopyrones.

Dioxide of 2-methyl-1-thiopyran-4-one (VII). 8 grams of anhydrous sodium acetate* and 150 ml of acetone were placed in a three-necked round-bottomed flask fitted with a stirrer and a reflux condenser. The suspension was vigorously stirred as it was heated on a water bath to the boiling point of acetone, and a suspension of 6 g of the dibromosulfone (I) in 100 ml of acetone was poured into the flask during the course of an hour. Then boiling was continued for another half-hour. The liquid turned brown. After it had cooled the sodium bromide was filtered out, and the solution was acidulated with strong hydrochloric acid until it was clarified. Then the sodium chloride was filtered out, and the acetone was driven off, the residue crystallizing. This yielded 2.5 g of the sulfone (VII). Two recrystallizations from alcohol yielded 2.2 g of the pure substance with an m.p. of 141-141.5° (72% of the theoretical yield).

4.035 mg substance: 6.785 mg CO_2; 1.460 mg H_2O; 2.450 mg SO_4. Found %: C 45.90; H 4.05; S 20.27. $C_6H_6O_3S$. Calculated %: C 45.75; H 3.83; S 20.27.

Dioxide of 2,5-dimethyl-1-thiopyran-4-one (VIII). 8.8 grams of the dibromosulfone (II), 10.8 g of sodium acetate, and 50 ml of acetone were stirred and heated together for one hour on a water bath (60-65°). Then the solution was cooled and treated as described in the preceding experiment. This yielded 4.1 g of crude crystals. Two recrystallizations from alcohol yielded 3.4 g of pure crystals of the sulfone (VIII), with an m.p. of 139° (15% yield).

4.675 mg substance: 8.365 mg CO_2; 2.048 mg H_2O. 4.325 mg substance: 7.720 mg CO_2; 1.848 mg H_2O. 5.790 mg substance: 10.362 mg CO_2; 2.495 mg H_2O; 3.250 mg SO_4. Found %: C 48.83, 48.69, 48.84; H 4.90, 4.77, 4.82; S 18.74. $C_7H_8O_3S$. Calculated %: C 48.84; H 4.68; S 19.06.

Heating an alcoholic solution of the sulfone (VIII) with hydroxylamine hydrochloride yielded the oxime with an m.p. of 177.5-178° (from water).

3.827 mg substance: 0.259 ml N_2 (23°, 738 mm). 5.942 mg substance: 0.400 ml N_2 (21°, 734 mm). Found %: N 7.58, 7.48. $C_7H_9O_3NS$. Calculated %: N 7.48.

Dioxide of 2,5-dimethyl-2,3-dihydro-1-thiopyran-4-one (IX). 1.3 grams of the bromosulfone (IV) (m.p. 141-143°), 0.9 g of anhydrous sodium acetate and 25 ml of acetone were stirred together for one hour on a water bath at 60-65°. The test product was then processed like the preceding one. Recrystallization from alcohol yielded 0.6 g of the sulfone (IX) with an m.p. of 112.5-113° (66% yield).

5.221 mg substance: 9.258 mg CO_2; 2,800 mg H_2O; 2.880 mg SO_4. 4.773 mg substance: 8.468 mg CO_2; 2.491 mg H_2O; 2.625 mg SO_4. Found %; C 48.39, 48.42; H 6.00, 5.84; S 18.41, 18.40. $C_7H_{10}O_3S$. Calculated %: C 48.28; H 5.75; S 18.41.

The semicarbazone of the sulfone (IX) had an m.p. of 232-233° (from water).

Dioxide of 2,5-dimethyl-5,6-dihydro-1-thiopyran-4-one (X). 1.5 grams of the bromosulfone (III) (m.p. 199-200°), 25 ml of acetone, and 1 g of anhydrous sodium acetate were stirred together for one

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[*] The crystalline sodium acetate, $CH_3COONa \cdot 3H_2O$, may also be used.

hour on a water bath at 60-65°. After it had cooled the solution was filtered and treated as described above, yielding 1 g of crude crystals. Two recrystallizations from alcohol yielded 0.75 g of the sulfone (X) with an m.p. of 95° (73% yield).

5.199 mg substance: 9.224 mg CO_2; 2.842 mg H_2O; 2.860 mg SO_4. 5.042 mg substance; 9.000 mg CO_2; 2.708 mg H_2O; 2.775 mg SO_4. Found %: C 48.42, 48.71; H 6.11, 6.01; S 18.36, 18.37. $C_7H_{10}O_3S$. Calculated %: C 48.28; H 5.75; S 18.41.

The semicarbazone of the sulfone (X) had an m.p. of 206-207° (from water).

4.198 mg substance: 6.340 mg CO_2; 2.153 mg H_2O. Found %: C 41.21; H 5.74. $C_8H_{13}O_3N_3S$. Calculated %: C 41.56: H 5.68,

Dioxide of 2-methyl-5,6,7,8-tetrahydro-1-thiochromen-4-one (XI). 2.8 grams of the dibromosulfone (V) (m.p. 186-187°), 2.8 g of sodium acetate, and 50 ml of acetone were stirred together for one hour on a water bath at 60-65°. Processing yielded 1.3 g of the sulfone (XI) with an m.p. of 87-87.5° (from alcohol), constituting an 80% yield.

4.166 mg substance: 8.632 mg CO_2; 2.074 mg H_2O; 1.895 mg SO_4. 5.585 mg substance: 11.590 mg CO_2; 2.885 mg H_2O; 2.549 mg SO_4. Found %: C 56.55, 56.63; H 5.70, 5.78; S 15.28, 15.23. $C_{10}H_{12}O_3S$. Calculated %: C 56.58; H 5.70; S 15.11.

Dioxide of 2-methylhexahydro-1-thiochromen-4-one (XII). 2.3 grams of the bromosulfone (VI) (m.p. 215-216°), 2.8 g of sodium acetate, and 100 ml of acetone were heated for one hour as described above. The solution was faintly colored. Processing yielded 1.2 g of the colorless sulfone (XII) with an m.p. of 118-118.5° (from alcohol). The yield was 70%.

3.934 mg substance: 8.095 mg CO_2; 2.336 mg H_2O; 1.736 mg SO_4. 4.595 mg substance: 9.420 mg CO_2; 2.620 mg H_2O; 2.030 mg SO_4. Found %: C 56.15, 55.94: H 6.64, 6.38; S 14.73. 14.75 $C_{10}H_{14}O_3S$. Calculated %: C 56.05; H 6.58; S 14.96.

III. Condensation of Divinyl with Dioxides of the γ-Thiopyrones

Dioxide of 2-methyl-5,8,9,10-tetrahydro-1-thiochromen-4-one (XIII). 2 grams of the sulfone (VII) (m.p. 139-140°), 4 g of butadiene, 20 ml of dioxane, and 0.02 g of pyrogallol were heated together to 150° for 4.5 hours in a steel ampoule. After the ampoule had cooled, it was opened, and 1.2 g of the condensation product was filtered out of the reaction mixture. Driving the dioxane off in vacuo yielded another 1.2 g of crystals with an m.p. of 174-175°. The aggregate yield was 92%. The sulfone (XIII) consisted of lustrous needles with an m.p. of 177-177.5° (from alcohol or aqueous dioxane).

4.416 mg substance: 9.195 mg CO_2; 2.259 mg H_2O; 2.000 mg SO_4. Found %: C 56.82 H 5.72; S 15.12. $C_{10}H_{12}O_3S$. Calculated %: C 56.58; H 5.70; S 15.11.

An experiment run at 200° yielded the same sulfone (XIII), but more highly contaminated with butadiene polymers.

Dioxide of 2,10-dimethyl-5,8,9,10-tetrahydro-1-thiochromen-4-one (XIV). 1 gram of the sulfone (VIII) (m.p. 138-139°), 2 g of butadiene, 11 ml of dioxane, and 0.01 g of pyrogallol were heated to 210-215° for 5 hours in a steel ampoule. Driving off the solvent yielded 1.1 g of the crude product. Two recrystallizations from alcohol yielded 0.8 g of the sulfone (XIV) with an m.p. of 101-102° (61% yield).

5.050 mg substance: 10.858 mg CO_2; 2.870 mg H_2O. 6.486 mg substance: 13.935 mg CO_2; 3.755 mg H_2O; 2.798 mg SO_4. Found %: C 58.68, 58.63; H 6.34, 6.48; S 14.40. $C_{11}H_{14}O_3S$. Calculated %: C 58.40; H 6.24; S 14.18.

An experiment run at 160° yielded a mixture of the initial sulfone (VIII) and the condensation product (XIV).

Dioxide of 2,10-dimethyl-5,8,9,10-tetrahydro-1-thiochroman-4-one (XV). 1.5 grams of the sulfone (IX) (m.p. 112-113°), 2.4 g of butadiene, 16.5 ml of dioxane, and 0.02 g of pyrogallol were heated together to 195-200° in a steel ampoule for 6 hours. After the ampoule had cooled, it was opened and the solvent driven off, which yielded 1.5 g of crystals with an m.p. of 116-147°. Fractional crystallization from alcohol divided the mixture into two fractions with m.p. of 175-178° and 117-118°, respectively.

Repeated recrystallization of the first fraction from alcohol yielded needles of the sulfone (XVa) with an m.p. of 194.5-195.5°.

4.802 mg substance: 10.174 mg CO_2; 3.030 mg H_2O. 4.538 mg substance: 9.622 mg CO_2: 2.910 mg H_2O; 1.960 mg SO_4. Found %: C 57.82, 57.86; H 7.06, 7.17; S 14.42. $C_{11}H_{16}O_3S$. Calculated %: C 57.87; H 7.06; S 14.04.

Repeated recrystallization of the second fraction from alcohol yielded crystals of the isomeric sulfone (XVb) with an m.p. of 127-128°.

3.902 mg substance: 8.328 mg CO_2; 2.552 mg H_2O; 1.618 mg SO_4. 4.570 mg substance: 9.713 mg CO_2; 2.965 mg H_2O; 1.985 mg SO_4. Found %: C 58.24, 58.00; H 7.32, 7.26; S 13.84, 14.50. $C_{11}H_{16}O_3S$. Calculated %: C 57.84; H 7.06; S 14.04.

Heating the sulfone (X) with butadiene. 1.4 grams of the sulfone (X) (m.p. 95°), 2.5 g of butadiene, 15.4 ml of dioxane, and approximately 0.02 g of pyrogallol were heated together in a steel ampoule for 4 hours at 200°. Driving off the solvent yielded 1.1 g of crystals with an m.p. of 94-94.5° (from alcohol). Their mixed melting point with the original sulfone (X) exhibited no depression. The substance recovered was reheated with butadiene for 4.5 hours at 200° under the same conditions as before. Driving off the solvent yielded 0.950 g of crystals with an m.p. of 94-95°. Their mixed melting point with the original sulfone (X) exhibited no depression.

SUMMARY

1. Heating solutions of dioxides of tetrahydro-γ-thiopyrones in glacial acetic acid with bromine produces high yields of the corresponding mono- and dibromosulfones (I-VI).

Heating the bromosulfones (I-VI) with sodium acetate in acetone readily splits off hydrogen bromide, producing the corresponding dioxides of the thiopyrones and dihydro-1-thiopyrones (VII-XII), the yields ranging from 70 to 80%.

3. The sulfones (VII) and (VIII) enter into condensation with butadiene at 150-200° in a dioxane solution, forming the sulfone (XIII) with a 92% yield and the sulfone (XIV) with a 61% yield, respectively.

4. Condensing the sulfone (IX) with butadiene at 200° results in a 65% yield of two isomeric cis sulfones (XVa) and (XVb), differing in their configuration at the second carbon atom.

5. The sulfone (X) does not enter into a diene syntheses at temperatures up to 200°.

6. The ability of dioxides of substitution derivatives of the γ-thiopyrones to enter into a diene synthesis depends upon the position of the substitutent in the ring. Introducing a methyl group at the α position to the carbonyl group greatly hampers diene condensation, while introducing the methyl group at the β position to the carbonyl group renders this condensation impossible at temperatures up to 200°.

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Received July 29, 1950

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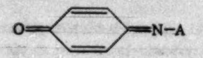
N-ARYL SULFONYLQUINONIMINES 1)

S. I. Burmistrov and E. A. Titov

In our opinion the study of the reactions of the quinonimines and quinodiimines and their derivatives is of tremendous theoretical significance. For the quinonimines and quinondiimines always appear as intermediate products in the syntheses of many classes of dyes, namely: the quinonimine dyes (indophenols and indamines), the azines, the oxazines, the thiazines, and some of the azomethine dyes. We are justified in saying that the quinonimines and quinondiimines play the same great role, one might say extremely important role, in the syntheses of the foregoing groups of dyes that diazonium salts play in syntheses of azo dyes. The quinonimines and quinondiimines possess properties that approach those of the diazonium salts: extremely high reactivity and, as a result, instability. They differ from the diazonium salts, however, in being nonionic.

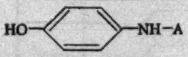
As we know, the N-acyl substitution derivatives of quinonimines (I) are equally nonionic compounds:


(I)

where A is an acid radical that can occur independently as the fairly stable anion A^-. Well-known members of this group of compounds are the quinonechlorimides and the quinonebromimides recently investigated by us [1,2]. These compounds do not contain an ionically bound halogen, but they can enter into reactions resembling the reactions of diazonium salts.

One of the most interesting reactions that link the quinonechlorimides to the diazonium salts, which is analogous to an azo coupling, is their reaction with phenols and amines, yielding indophenols and indamines. Determination of which N-substitution derivatives of the quinonimines can enter into the reaction in which indophenols are produced is of definite theoretical interest.

The formation of quinonebromimides and quinonebromodiimides and the reactions of the latter with phenols have led one of the present authors to describe a convenient specific reaction for p-aminophenols and p-diamines [2,3]. Observations of the quinonebromimide reaction of the N-aryl substitution derivatives of aminophenols indicated that the ordinary acyl substitution derivatives of p-aminophenol (II):


(II)

such as N-acetyl-1,4-aminophenol ($A = CH_3CO$) or N-benzoyl-1,4-aminophenol ($A = C_6H_5CO$) do not exhibit the quinonebromimide reaction. The N-aryl sulfonyl-1,4-aminophenols, which formed indophenols in the quinonebromimide reaction, in contrast to the compounds mentioned above, constituted an inexplicable exception at first sight. Since we could not suppose that the aryl sulfonyl radical would be split off and a quinonebromimide formed under the conditions of the quinonebromimide reaction, we assumed that N-aryl sulfonylquinonimines, which were able to react with the phenols and form indophenols, were produced in a simple oxidation reaction. We therefore chose as the objective of the present research the synthesis of the hitherto unknown N-aryl sulfonylquinonimines and a study of their properties. Our investigations resulted in the synthesis of some representatives of a new class of compounds (III).

$$O{=}Ar''{=}N{-}SO_2Ar \quad \text{(III)}$$

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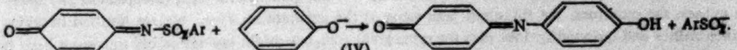
1) Compounds containing the =NH group are named differently in the literature: as imines and as imides. In the Beilstein handbook the single terminology: imides, has been adopted; it did not persist, however. We have retained the latter term solely for N-halogenated imines.

where Ar* is an aromatic group, an arylene, a constituent of the quinonimine residue, and Ar is an aromatic radical, an aryl. The synthesis was effected by oxidizing the N-aryl sulfonyl-1,4-aminophenols (II) with bichromate in the cold in dilute sulfuric acid.

The synthesized compounds proved to be yellow or yellow-orange crystalline substances, in contrast to the quinonechlorimides and quinonebromimides, they resisted heat fairly well and therefore exhibited sharp melting points. Noteworthy among the other properties of the substances we synthesized was their indophenol reaction, that is, the appearance of a blue (or violet) coloration when reacted with phenol or 1-naphthol in an alkaline medium. We made a thorough study of this reaction, finding that N-aryl sulfonylquinonimines react with phenol in an alkaline medium by splitting off the aryl sulfonyl residue as an anion of an aryl sulfinic acid. The stoichiometric equation for this transformation may be written as follows:

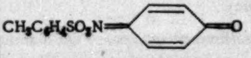
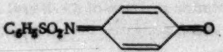
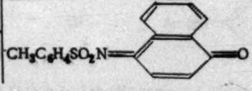


(IV)

The N-aryl sulfonylquinonimines we investigated can be readily reconverted into aryl sulfonylaminophenols by the action of reducing agents. Derivatives of 1,4-benzoquinone react quantitatively with potassium iodide in an acid medium liberating iodine. This latter reaction was utilized to identify the compounds by determining their oxidation equivalents.

An aryl sulfonylquinonimine and an N-aryl sulfonyl-1,4-aminophenol constitute a reversible oxidation-reduction system, like the quinone-hydroquinone system. In contrast to the quinones, aryl sulfonylquinonimines are not colored by acetoacetic ester in ammonia. When aryl sulfonylquinonimines are heated with 20% sulfuric acid, they decompose, yielding quinone. The properties of the synthesized compounds are given in the following table.

Properties of N-Aryl Sulfonylquinonimines

No.	Name	Formula	Melting point	Indophenol reaction	
				With phenol	With 1-naphthol
1	N-p-Toluenesulfonyl-1,4-benzoquinonimine	 CH$_3$C$_6$H$_4$SO$_2$N=	126.5°	Blue	Violet
2	N-Benzenesulfonyl-1,4-benzoquinonimine	 C$_6$H$_5$SO$_2$N=	137	″	″
3	N-p-Toluenesulfonyl-1,4-naphthoquinonimine	 CH$_3$C$_6$H$_4$SO$_2$N=	156	—	Blue

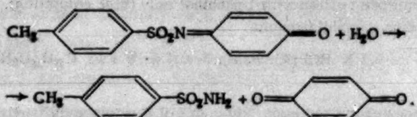
As may be readily seen, aryl sulfonylquinonimines exhibit the same indophenol reaction as the quinonebromimides [2].

EXPERIMENTAL

The N-aryl sulfonyl-1,4-aminophenols required for synthesizing the aryl sulfonylquinonimines were prepared by acylating 1,4-aminophenols with the respective aryl sulfochlorides in a water-soda suspension.

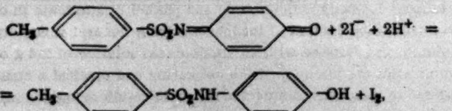
N-p-Toluenesulfonyl-1,4-aminophenol. 84.8 grams of soda (0.8 mole – 100% excess) was dissolved in 400 ml of water, 64.2 g (0.40 mole) of 1,4-aminophenyl hydrochloride was added to the soda solution, and then 76.2 g (0.4 mole) of p-toluene sulfochloride was added at room temperature. The mixture was refluxed on a water bath and constantly stirred with a mechanical stirrer until the odor of toluene sulfochloride had disappeared, which took 2.5 hours. When the reaction was over, the mixture was cooled, and the precipitated toluenesulfonyl derivatives were filtered out, washed with water, and dried. The yield was nearly quantitative (103 g). The substance was purified by recrystallizing it from a large quantity of water; the m.p. of the recrystallized product was 144.5°, the literature giving the m.p. of N-p-toluenesulfonyl-1,4-hydroxyanilide as 143° [4].

N-p-Toluenesulfonyl-1,4-benzoquinonimine. 10 grams of finely pulverized N-p-toluenesulfonyl-1,4-aminophenol was added at room temperature to a solution of 5.7 g of sodium dichromate ($Na_2Cr_2O_7 \cdot 2H_2O$) in 175 ml of 20% sulfuric acid. The mixture was stirred for 50 minutes and then diluted with water, the precipitate being filtered out. The precipitate was washed on the filter with water and finally washed with alcohol to eliminate part of the unreacted toluenesulfonyl-1,4-aminophenol. The yield ranged from 7.9 to 8.4 g. or 79%-84% of the theoretical. Refining is best accomplished by crystallization in small portions from alcohol, taking care to avoid prolonged heating in the alcohol solution, as we found that aryl sulfonylquinonimines are reduced when heated for a long time in alcohol, while the alcohol is oxidized, as is noticeable by the odor of acetaldehyde. The refined crystalline product had an m.p. of 126.5°. Analysis indicated that it contained sulfur and nitrogen. Orange-yellow crystals that turned into a yellow powder when pulverized; freely soluble in ether, benzene, and glacial acetic acid, slightly soluble in cold alcohol, more soluble in hot alcohol, and very slightly soluble in water. In ammonia, it colored phenol blue and 1-naphthol violet. The reaction involved in the production of indophenols was rapid at room temperature. Heating with 20% sulfuric acid on a water bath yielded 1,4-benzoquinone, which was distilled with steam. The distillate was an aqueous solution with the odor of quinone; it is turned blue by acetoacetic ester and ammonia: the quinone reaction [5]. It is likely that in the first stage of acid hydrolysis 1,4-benzoquinone and p-toluenesulfamide are produced:



Since the initial toluenesulfonyl-1,4-aminophenol was very readily soluble in alcohol, washing with alcohol was a convenient method of separating the unoxidized compound from the oxidized one. Oxidation with chromic anhydride in glacial acetic acid produced an 80% yield of toluenesulfonylquinonimine. Attempts to secure this product by oxidizing with a suspension of lead dioxide in benzene met with failure, the yields being extremely low.

The product was analyzed by determining its oxidation equivalent. This was done by dissolving a sample of the toluenesulfonylquinonimine in alcohol, and adding 20% sulfuric acid and an excess of potassium iodide. The iodine liberated in the stoichiometric equation:



was back-titrated with thiosulfate. After the thiosulfate titration colorless thin needles settled out; they were filtered out and dried, and exhibited the melting point of the original toluenesulfonyl-1,4-aminophenol.

0.1993 g substance: 15.13 ml 0.1 N $Na_2S_2O_3$. 0.2002 g substance: 15.14 ml 0.1 N $Na_2S_2O_3$. Found: equiv. 131.7, 132.1. $\frac{1}{2}C_{13}H_{11}O_3NS$. Calculated: equiv. 130.65. 0.1993 g substance: 7.70 ml 0.1 N HCl (Kjeldahl) Found %: N 5.41. $C_{13}H_{11}O_3NS$. Calculated %: N 5.36.

N-Benzenesulfonyl-1,4-aminophenol. This was similarly prepared from 1,4-aminophenol hydrochloride and benzene sulfochloride. Crystallization from water yielded barely pinkish flat needles, m.p. 155°. The literature gives m.p. 153° [6] and 156.5° [7]. They are very freely soluble in cold alcohol.

N-Benzenesulfonyl-1,4-benzoquinonimine. 10 grams of benzenesulfonyl-1,4-aminophenol was ground to a powder and added to a solution of 6 g (50% excess) of sodium dichromate ($Na_2Cr_2O_7 \cdot 2H_2O$) in 180 ml of 20% sulfuric acid. The mixture was stirred vigorously for 1 hour 15 minutes, then diluted with water to make 400 ml, and the precipitate filtered out. The dry precipitate weighed 7 g (70% of the theoretical) after it had been washed with water until its reaction was neutral to eliminate the acid and with alcohol to eliminate the unoxidized product. Further purification followed the lines of the preceding synthesis, employing careful crystallization from alcohol. This yielded orange-yellow crystals, or a yellow powder, m.p. 137°, which contained sulfur and nitrogen. It was freely soluble in ether, benzene, and glacial acetic acid, and slightly soluble in cold alcohol. It colors phenol blue and 1-naphthol violet. It stains the skin brown, like quinonechlorimide and quinonebromimide. The synthesized compound was analyzed by determining its oxidation equivalent by titrating the iodine liberated from potassium iodide in an acid medium with thiosulfate and then determining the nitrogen by the Kjeldahl method:

0.0684 g substance: 5.32 ml 0.1 N $Na_2S_2O_3$. 0.0644 g substance: 5.02 ml 0.1 N $Na_2S_2O_3$. Found: equiv. 128.4, 128.5. $\frac{1}{2}C_{12}H_9O_3NS$. Calculated: equiv. 123.65. 0.2143 g substance: 8.77 ml 0.1 N HCl (Kjeldahl). Found %: N 5.73. $C_{12}H_9O_3NS$. Calculated %: N 5.67.

N-p-Toluenesulfonyl-1,4-aminonaphthol. 19.9 grams of 1,4-aminonaphthol hydrochloride, produced by the method [8] was added to a solution of 21.2 g of soda (0.2 mole) in 400 ml of water. After some time had passed, 19.1 g of p-toluene sulfochloride was added at room temperature. The whole was vigorously stirred as its temperature was raised to 70°, being kept at that temperature until the odor of toluene sulfochloride had disappeared (about 2.5 hours). Then the precipitate was filtered out, washed with water, and dried. It was refined by recrystallization from xylene. This yielded pinkish-gray crystals that were readily soluble in alcohol, slightly soluble in cold benzene and xylene, more so in hot xylene, and insoluble in water. M.p. 183°. Qualitative analysis indicated that sulfur and nitrogen were present. The substance exhibited the quinonebromimide reation with 1-naphthol only (blue coloration), while a paper test showed that it combined with 4-nitrophenyldiazonium.

0.2705 g substance: 8.55 ml 0.1 N HCl (Kjeldahl). Found %: N 4.43. $C_{17}H_{15}O_3NS$. Calculated %: N 4.47.

N-p-Toluenesulfonyl-1,4-naphthoquinonimine. 10 grams of N-p-toluenesulfonyl-1,4-aminonaphthol was placed in a solution of 4.75 g of sodium dichromate ($Na_2Cr_2O_7 \cdot 2H_2O$) in 145 ml of 20% sulfuric acid. After the mixture had been stirred for 3 hours at room temperature, the precipitated oxidized product was filtered out and washed with water and then with alcohol. Crystallization from alcohol yielded red-yellow lamellae, m.p. 156°. Freely soluble in benzene, very slightly soluble in cold alcohol, and insoluble in water. In contrast to the previous two compounds, it does not liberate iodine quantitatively from potassium iodide and does not color phenol in ammonia, though it does color 1-naphthol blue, like 1,4-naphthoquinonebromimide.

0.2001 g substance: 6.53 ml 0.1 N HCl (Kjeldahl). Found %: N 4.57. $C_{17}H_{13}O_3NS$. Calculated %: N 4.50.

Study of the indophenol reaction of N-toluenesulfonyl-1,4-benzoquinonimine. We investigated the reaction products of toluenesulfonyl-1,4-benzoquinonimine and phenol in ammonia in order to explore the stoichiometric equation governing the production of indophenols from the aryl sulfonylquinonimines. 4.36 g of N-p-toluenesulfonylquinonimine was agitated with an ammoniacal solution of 2.4 g of phenol. This produced a strong blue coloration. After the intensity of the coloration had reached a constant value, the ammoniacal solution was filtered to remove the unreacted N-p-toluenesulfonylquinonimine. The solution was then carefully neutralized with acetic acid to eliminate the indophenol produced. The red-brown precipitate was filtered out, the dissolved indophenol being extracted with benzene. The red-brown precipitate had an m.p. of 59°; the m.p. being raised to 160° after crystallization from acetone. The substance exhibited all the properties of the indophenol (IV).

The literature gives the m.p. of the indophenol with this structure as 160° [9]. It dissolves in ammonia and alkali, coloring them blue.

After the indophenol had been extracted with benzene, the aqueous layer was acidulated and then extracted with ether. Evaporation of the ether yielded pinkish crystals with an m.p. of 85°. The m.p. of p-toluenesulfinic acid is 86° according to the literature [10]. p-Thiocresol was produced by reduction with zinc and sulfuric acid in order to prove that the synthesized product was the same as p-toluenesulfinic acid. We secured a solution that had the intense odor of thiocresol. The thiocresol was driven off with steam. The recovery of indophenol and p-toluenesulfinic acid from the reaction medium confirmed the stoichiometric equation given in the preceding theoretical section for the formation of indophenols from aryl sulfonylquinonimines. Hence, the aryl sulfonyl residue is split off as an anion of an aryl sulfinic acid, as demonstrated above. This is all the more remarkable inasmuch as it is ordinarily very difficult to split an aryl sulfonyl residue from its bond to a nitrogen atom. In this instance the cleavage is effected by extremely weak agents in the cold.

SUMMARY

1. Three N-aryl sulfonylquinonimines have been synthesized for the first time, and their properties and reactions are described.

2. N-Aryl sulfonylquinonimines that are derivatives of 1,4-benzoquinone liberate iodine quantitatively from iodides in an acid solution.

3. The N-aryl sulfonylquinonimines react with phenol and 1-naphthol, yielding indophenols, the aryl sulfonyl residue splitting off as an anion of an aryl sulfinic acid.

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Received October 16, 1950

Ivanovo Institute of Chemical Technology

3. Three previous investigations [illegible] for the last three, and their [illegible] are confirmed.

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(6) German Patent [illegible]

(7) [illegible] J. Am. Chem. Soc. [illegible]

(8) [illegible] Critical Tables, Vol. [illegible]

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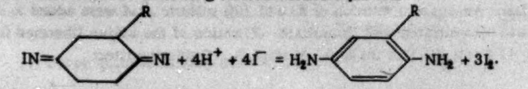
Received October 26, [illegible]

QUINONIODIMIDES AND QUINONEDIIODODIIMIDES [1)]

S. I. Burmistrov and V. I. Glaskov

In connection with the general plan of our research on the properties and reactions of N-substitution derivatives of the quinonimines, we described quinonebromimides and quinonedibromodiimides [1,2] and N-aryl sulfonylquinonimines [3] in our previous papers. The present research deals with the synthesis and an investigation of the properties and reactions of the hitherto undescribed quinone-N-iodimides and quinone-N,N'-diiododiimides. As might have been expected, it was much harder to synthesize the latter compounds because of the lower stability of the substances investigated. To this there were added the difficulties arising from the low stability of alkaline solutions of the hypoiodites. We have synthesized three quinonediiododiimides and secured them in the individual state; in an attempt to synthesize 1,4-benzoquinoneiodimide we secured a yellow crystalline substance that decomposed rapidly, turning dark and giving off iodine. This made it impossible to isolate it or analyze it. We proved that the unstable compound was 1,4-benzoquinoniodimide by demonstrating the existence of the indophenol reaction (formation of blue indophenols with alkaline solutions of phenol) and then by analyzing the benzene solutions for their iodine content by the iodate method and by determining their oxidative titer.

The synthesized quinonediiododiimides proved to be more intensely and deeply colored than the analogous quinonedichlorodiimides and quinonedibromodiimides; like the latter, they react with phenols in an alkaline solution, producing intensively colored indophenols. Like the quinonedibromodiimides, the quinonediiododiimides, as derivatives of quinones with a high oxidation potential, liberate iodine quantitatively from acid solutions of iodides in accordance with the following stoichiometric equation:



This reaction was employed to analyze and identify the quinonediiododiimides. The quinonediiodidiimides are much less soluble in nonpolar solvents than the analogous quinonedibromodiimides and are light-sensitive. As might be expected the low stability of the quinonediiodidiimides is due to the slight energy of the N—I bond; that is why comparatively little energy is required to cleave them, yielding free atoms of iodine.

The following table gives the properties of the synthesized quinoniodimide and quinonediiododiimides.

EXPERIMENTAL

Owing to the instability of the compounds mentioned, rapid operations at solution temperatures of the order of 0° are essential conditions for their successful isolation. The following procedure was employed to prevent decomposition of the hypoiodite: finely pulverized iodine was added to a chilled alkali solution, and then the solution of aminophenol or of the p-diamine, was rapidly added, with stirring, without waiting for the iodine to dissolve, the resultant precipitate being quickly filtered out on a suction filter and washed with water and then with ether.

1,4-Benzoquinoniodimide. Because the free compound is so unstable, only benzene solutions of it were secured, the solutions being analyzed as set forth below.

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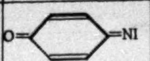
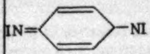
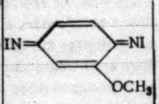
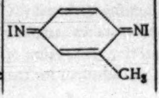
1) Compounds containing the =NH group are named differently in the literature: as imines and as imides. In the Beilstein handbook the latter term is used throughout, but it did not persist in the chemical literature, however. We have retained the latter term solely for N—halogenated imines (quinonechlorimides, quinonebromimides, etc.)

Properties of Quinoniodimide and Quinonediiododiimides

No.	Name	Formula	Decomposition temp.	Appearance
1	Benzoquinoniodimide			Reddish-yellow crystals
2	1,4-Benzoquinonediiododiimide		60°	Golden-yellow crystals
3	2-Methoxy-1,4-benzoquinonediiododiimide		65	Yellow crystals
4	2,5-Toluquinonediiododiimide		77	Reddish-yellow crystals

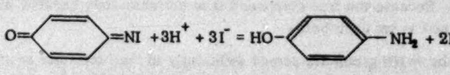
A solution of 6.5 g of NaOH (0.16 mole) in 115 ml of water was chilled to −5° and stirred mechanically while 10.2 g (0.04 mole) of finely powdered iodine was added. A previously prepared solution of 1.09 g (0.01 mole) of 4-aminophenol in 100 ml of water + 2 g of NaOH was then immediately added to the alkaline suspension of iodine, a reddish-yellow precipitate settling out. Benzene was added to extract the quinoniodimide, and the mixture was agitated. After the crystals had dissolved in the benzene, the benzene solution was separated, washed with water, and dried with calcium chloride. The yellow benzene solution was fairly stable: for analysis it was diluted with more benzene in order to obtain a 1/40-molar solution, based on 1,4-benzoquinoniodimide.

The presence of 1,4-benzoquinoniodimide in the benzene solution was proved by the following qualitative reactions: a drop of the benzene solution applied to paper turned an intense blue when treated with phenol in ammonia; the colored benzene solutions were decolorized by reducing agents. We determined the oxidative titer and the percentage of iodine by the iodate method in order to prove that the solution contained 1,4-benzoquinoniodimide.

Determination of the oxidative titer. An Aqueous solution of KI and 10% sulfuric acid were added to the benzene solution. The liberated iodine was back-titrated with thiosulfate. Titration of the iodine liberated from 20 ml of the benzene solution consumed: I) 11.2 ml; II) 11.2 ml of 0.1 N $Na_2S_2O_3$. Oxidative titer: $\frac{11.2\cdot 0.1}{20} = 0.056$ mg-equivalent per ml.

Determination of the iodine [4]. 15 ml of a 20% alcoholic solution of KOH was added to 20 ml of the benzene solution, the mixture was boiled for 10 minutes, and the alcohol and benzene were evaporated in a porcelain dish. The residue was calcined and dissolved in water, the solution being diluted to 100 ml in a 100-ml measuring flask. 50 ml of the resultant aqueous solution was neutralized with acid, an excess of chlorine water being added to convert the iodide into an iodate. The solution was heated and then boiled to eliminate the excess chlorine. After the excess chlorine had been driven off, KI and 10% sulfuric acid were added. The liberated iodine was back-titrated with thiosulfate. 10 ml of the original benzene solution (allowing for the dilution) required the following amounts of thiosulfate: Test I: 8.3 ml of 0.1 N $Na_2S_2O_3$; Test II: 8.5 ml of 0.1 N $Na_2S_2O_3$. Whence the amount of iodine (as a compound) was: Test I: $\frac{8.3\cdot 0.1}{6\cdot 10} = 0.0138$ mg-atom per ml; Test II: $\frac{8.5\cdot 0.1}{6\cdot 10} = 0.0141$ mg-atom per ml.

The analysis shows that each gram-atom of iodine in the compound corresponds to 4 oxidation equivalents. The only possible explanation of this is that the solution contains quinoniodimide, which reacts with the iodide in an acid solution as follows:



We have thus proved that the benzene solution contains 1,4-benzoquinoniodimide.

1,4-Benzoquinonediiododiimide. A solution of 13 g (0.32 mole) of NaOH in 50 ml of water was chilled to 0° and 20.3 g of finely powdered iodine (0.08 mole) was added. A solution of 1.08 g (0.01 mole) of 1,4-phenylenediamine in 100 ml of water was added at once to the suspension. The golden-yellow precipitate was filtered out quickly, washed with water, then with ether. Attempts to crystallize the substance were fruitless: it broke down, yielding iodine. The dried precipitate was used for analysis. This was done by dissolving a sample of the substance in benzene and adding an aqueous solution of potassium iodide and 10% sulfuric acid, the iodine liberated being back-titrated with thiosulfate. The equation for this reaction is given in the theoretical section of this paper.

0.0368 g subs.: 6.8 ml 0.1 N $Na_2S_2O_3$. 0.1386 g subs.: 24.2 ml 0.1 N $Na_2S_2O_3$.
Found: equiv. 58.9, 60.9. $\frac{1}{6}C_6H_4N_2I_2$. Calculated: equivalent 59.66.

2-Methoxy-1,4-benzoquinonediiododiimide. The 2,5-diaminoanisole required for this synthesis was prepared by reducing 5-nitro-2-aminoanisole with zinc dust in an aqueous-alcoholic solution containing NaCl, as described in a previous paper [2]. The excess zinc dust and the zinc oxide were filtered out of the solution, which was then diluted with water so as to produce an approximately half-molar solution of 2,5-diaminoanisole. 20 ml of this solution was added, as before, to a suspension of 20.3 g of finely powdered iodine in a solution of 13 g of NaOH in 200 ml of water. It was found advisable to employ more highly diluted solutions than indicated for the synthesis of 1,4-benzoquinonediiododiimide. The yellow precipitate was quickly filtered out and washed with water. The precipitate was purified by dissolving it in dichloroethane at 35°, filtering out the undissolved impurities, shaking with calcium chloride to remove the water, and chilling to −15°. The precipitated yellow crystals were filtered out rapidly and dried. The substance breaks down when heated to 65°; it colors phenol in ammonia blue; and it colors 1-naphthol blue, thus differing from the preceding compounds. It was analyzed by determining its oxidation equivalent.

0.0516 g subs.: 8.5 ml 0.1 N $Na_2S_2O_3$. 0.0941 g subs.: 15.4 ml 0.1 N $Na_2S_2O_3$.
Found: equiv. 66.6, 66.3. $\frac{1}{6}C_7H_6ON_2I_2$. Calculated: equiv. 64.66.

2,5-Toluquinonediiododiimide. The 2,5-diaminotoluene required for the synthesis was prepared by reducing 5-nitro-2-aminotoluene as indicated above [2]. The aqueous solution was employed as it was in synthesizing the diiododiimide, the remainder of the synthesis procedure resembling that outlined above. Crystallization from dichloroethane yielded the substance as reddish-yellow crystals. It decomposes when heated to 77°. It colors phenol in ammonia blue. It was analyzed by determining its oxidation equivalent.

0.0274 g subs.: 4.8 ml 0.1 N $Na_2S_2O_3$. 0 0788 g subs.: 13 4 ml 0.1 N $Na_2S_2O_3$.
Found. equiv 62.1, 64 0. $\frac{1}{6}C_7H_6N_2I_2$. Calculated: equiv. 62.0.

SUMMARY

1. Three quinonediiododiimides, constituting a new class of compounds, have been synthesized for the first time.

2. It has been proved that when p-aminophenol is reacted with hypoiodite, 1,4-benzoquinoniodimide is produced.

3. The physical properties and the reactions of the new compounds have been described.

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[3] S. I. Burmistrov and E. A. Titov. J. Gen. Chem., 22, 999 (1952); see Consultants Bureau translation, p. 1053.

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Received October 16, 1950

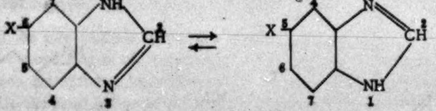
Ivanovo Institute of Chemical Technology

RESEARCH ON IMIDAZOLE DERIVATIVES

III. NITRATION OF DERIVATIVES OF BENZIMIDAZOLE AND SYNTHESIS OF SOME NEW DERIVATIVES OF 1,2,4,5-DIIMIDAZOLOBENZENE [1]

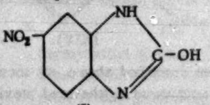
L. S. Efros

When doing research on the behavior of benzimidazole and its derivatives in substitution reactions, the first thing we must bear in mind is the tautomerism of these compounds, manifested in the fact that the hydrogen in the imino group of the heterocyclic ring can shift from one nitrogen atom to another. Such a tautomeric shift of the hydrogen atom causes no change in the molecule of the unsubstituted benzimidazole, but ought to yield two different compounds when it occurs in asymmetrical derivatives of the latter:

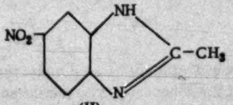


This is why these substances are given a dual name in F.F.Beilstein's well-known handbook and in many scientific papers, as an indication that they can occur in both tautomeric forms. No instance of desmotropism of benzimidazole derivatives has been described in the literature up to now, however, which is an obvious indication of the great ease with which one substance is converted into the other. The reason for this, in our opinion, is the amphoteric nature of the compounds in question, so that the tautomeric shift can occur in an acid or an alkaline medium.

In the present report we have attempted to settle the question of the effect exerted by the tautomerism of the imidazole group upon the benzene ring when benzimidazole derivatives are nitrated. In this reaction, which takes place in an acid medium, the benzimidazole derivatives must act as cations, in which the equivalent nitrogen atoms of the heterocyclic ring can transfer their electrons to para and ortho positions of the benzene ring, thus facilitating the entrance of electronophilic substituents. Actually, benzimidadole and its 2-substitution derivatives are nitrated extremely easily, as several researchers had discovered long before our investigations [2], the nitro group entering at the 5 and 6 positions of the benzimidazole group exclusively, these being para positions with respect to the nitrogen atoms of the heterocyclic ring. Whenever one of these positions is occupied by a Class I substituent, such as methyl, methoxy, or acetylamino group, the nitro group selectively enters the other free para position to the 5 or 6 nitrogen atom of the heterocyclic ring [3]. In the light of these findings the results of the research by Kym and Ratner [4], who made a study of a second nitration of 2-hydroxy-5-nitrobenzimidazole (I) and of 2-methyl-5-nitrobenzimidazole (II), seem to be quite unexpected.

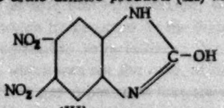


(I)



(II)

These researchers discovered that the compound (I) enters into this reaction with great ease, while the compound (II) requires rather severe conditions, the nitro group entering these compounds at the 5 (or 6) position as before, producing the ortho dinitro products (III) and (IV).



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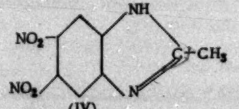
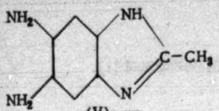


(IV)

Wishing to check these findings, we readily synthesized 5,6-dinitro-2-methylbenzimidazole (IV) and reduced it to the corresponding diamine (V). We then employed the method of condensing ortho diamines with carboxylic acids under pressure in the presence of hydrochloric acid described by us previously, which results in the formation of imidazole rings [5], to secure high yields of the previously described [4] methyl- and dimethyldiimidazolo-1,2,4,5-benzene (VI) and (VII).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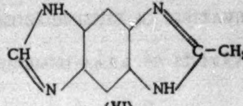
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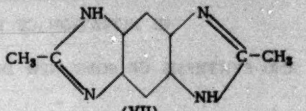
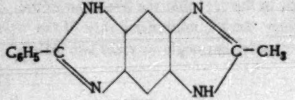

(VII)

The similarly constructed derivatives of diimidazolo-1,2,4,5-benzene: (VIII), (IX), (X), and (XI), not described in the literature before, were synthesized under the same conditions, by condensing the diamine (V) with benzoic, phenylacetic, phenylpropionic, and 2-phenylbenzimidazole-5-carboxylic acids, respectively, the yields being uniformly satisfactory.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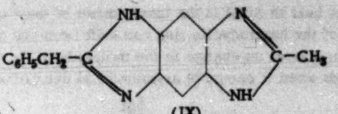
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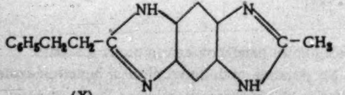
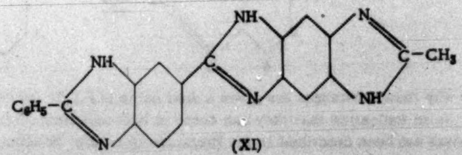
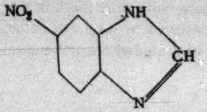
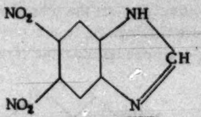

(X)

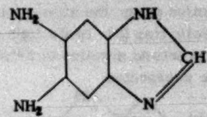

(XI)

It might have been thought that the unexpected course taken by the nitration reaction in the case of the compounds (I) and (II) was somehow related to the influence of the substituents located at the 2 position [6]. We therefore thought it important to study the nitration of unsubstituted benzimidazole, which we proceeded to do.

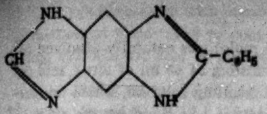
By nitrating benzimidazole under conditions that differed somewhat from those described in the literature [7] we readily obtained the mononitro derivative (XII), to which another nitro group could be added when the conditions were severe enough; separating the dinitro product (XIII) from the unreacted mononitro derivatives involved considerable difficulty, however. Reducing the compound (XIII) by tin and hydrochloric acid, we obtained the corresponding diamine (XIV), which we could not secure in the chemically pure state owing to its extraordinarily low resistance to oxidation.


(XII)

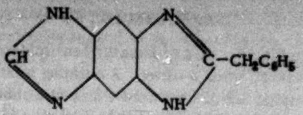

(XIII)


(XIV)

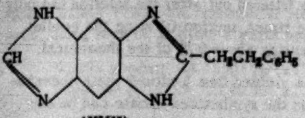
But, by condensing this compound with acetic acid under the conditions described above, we secured a good yield of a derivative of diimidazolo-1,2,4,5-benzene (VI), identified with the compound synthesized previously by condensing the diamine (V) with formic acid. This confirmed the structure of the dinitro product (XIII). Condensing the diamine (XIV) with benzoic, phenylacetic, phenylpropionic, and 2-phenylbenzimidazole-5-carboxylic acid yielded the derivatives of diimidazolo-1,2,4,5-benzene (XV), (XVI), (XVII), and (XVIII), respectively, which have not been described previously, and were purified as their hydrochlorides:



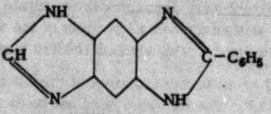
(XV)



(XVI)



(XVII)



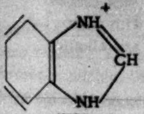
(XVIII)

Hence, the singular course of the nitration of benzimidazole derivatives cannot be attributed to the influence of the substituent at the 2 position. It is likewise obvious that the substituent present in the benzene ring of benzimidazole has no decisive effect upon the course of this reaction in the cases considered. Benzimidazole evidently cannot be regarded merely as a derivative of benzene that contains two substituents in an ortho position to each other. This compound, like, say, naphthalene, possesses its own singularities, which are manifested in the nitration reaction, governing its direction, and consist of the following: 1) the 5 and 6 positions are more reactive than the 4 and 7 positions; and 2) the 5 and 6 positions behave only very slightly as ortho positions, in this respect resembling the 2 and 3 positions of naphthalene.

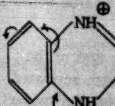
It seems to us that the sole explanation for the origin of these specific peculiarities is the fact that the imidazole group deforms the benzene ring of the benzimidazole considerably, destroying its symmetry. This gives rise to a double linkage between the carbon atoms common to the benzene and imidazole rings as well as between the 4-5 and 6-7 positions, while the bond between the 5 and 6 carbon atoms tends to become a single bond (XIX).

With this arrangement of the bonds, benzimidazole ought to have chemical properties that resemble those of naphthalene. In contrast to the latter, however, our compound exhibits higher reactivity at the 5 and 6 positions instead of the 4 and 7 positions, though the former positions correspond to the less active β-positions in naphthalene. The reason for this singularity in benzimidazole is the orienting effect of the nitrogen atoms in the heterocyclic ring, which is transmitted via the chain of conjugated bonds. The 5 and 6 positions prove to be the reactive ends of the chain because, we believe, there is some break in conjugation between these positions (XX).

If there is any substituent present at one of these positions, say, 5, it can exert influence only toward the 4 position, its influence upon the 6 position, which is linked to the 5 position by a single bond, being very slight. If the substituent is a Class II one, such as a nitro group, the succeeding substituent can enter at the 6 position, as we have demonstrated previously. But if the substituent attached to the 5 position is a Class I one, we ought to find discordant orientation present: whereas this substituent promotes the reaction at the 4 position most, the imino group in the heterocyclic ring promotes a reaction at the 6 position. In this case the substituting group can evidently enter at both of these positions, though this depends upon the strength of the effect exerted by the Class I substituent already present. This is fully borne out by the findings in the literature. When 5-chloro- or 5-methyl- or 5-ethoxybenzimidazole is nitrated with potassium nitrate, for example, we can readily obtain [8] 4,6-dinitro derivatives, the first nitro group being added at the 6 position.



(XIX)



(XX)

The experiments of K. Fries and his co-workers [9] on the chlorination and bromination of derivatives of 5-hydroxybenzimidazole demonstrated that the first halogen atom enters at the 4 position, position 6 being substituted only later. Thus, the effect of the hydroxy group is greater in this case than the specific activity of the 6 position of the benzimidazole group. Fries also discovered the great readiness with which benzimidazole derivatives produce 4,5-quinones, and the impossibility of producing a quinone at the 5 and 6 positions, which is further confirmation of our hypothesis concerning the deformation of the benzene ring in this compound.

It is worthy of note that Fries himself, who performed these experiments in order to compare benzimidazole with naphthalene, which he depicted by the Erlenmeyer formula, came very close to our picture of the structure of this heterocyclic compound. Fries believed, however, that in this case the properties of these two compounds ought to be fully similar, which was not the case, of course. Whereas it is the α-positions that are most active in naphthalene [10], it is the 5 and 6 positions that are most active in benzimidazole. Failing to get to the bottom of this intricate complex of problems, Fries had to abandon this conception.

EXPERIMENTAL

Nitration of 2-methylbenzimidazole. 66 g of 2-methylbenzimidazole (0.5 mole) was carefully dissolved in 200 ml of conc. sulfuric acid in a beaker, using a stirrer. A nitrating mixture, consisting of 40 ml of nitric acid (sp. gr. 1.4) and 60 ml of sulfuric acid (sp.gr. 1.84), was added a drop at a time to the resulting solution, whose temperature was not allowed to rise above 25-30°. Fifteen to twenty minutes after this addition was complete the nitro mass was carefully poured into cold water (1 liter), and 160 ml of 50% nitric acid was added to the resulting solution. The white needles of 5-nitro-2-methylbenzimidazole nitrate that settled were filtered out after the solution had fully cooled, pressed out well, washed with small portions of ice water two or three times, suction-filtering the needles thoroughly each time, and dried. This yielded 108-112 g of product, representing about 90% of the theoretical.

Careful treatment of an aqueous solution of this nitrate with ammonia yielded free 5-nitro-2-methylbenzimidazole, with a m.p. of 219°. The free base need not be isolated, however, as the synthesized nitrate can be employed for the second nitration.

This was done by dissolving 50 g of the 5-nitro-2-methylbenzimidazole nitrate in 50 ml of conc. sulfuric acid, adding 100 ml of nitric acid (sp.gr. 1.52), and refluxing for one hour. The mass was then poured out into 500 ml of water containing ice, and the slightly soluble nitrate was filtered out. Some more of the product (2-5 g) could be recovered as a base from the mother liquor by neutralizing it with ammonia. All the product was converted into a base, carefully neutralizing its solution in 250 ml of water with ammonia and filtering after it had cooled. The 5,6-dinitro-2-methylbenzimidazole was separated from the initial 5-nitro-2-methylbenzimidazole by making use of the very sparing solubility of the hydrochloride of the former in aqueous hydrochloric acid solutions. This was done by dissolving the synthesized base in 250 ml of boiling water, adding hydrochloric acid a drop at a time, using no excess, filtering the solution, and then adding an equal volume of conc. hydrochloric acid to it. This precipitated the hydrochloride of the dinitroproduct, which was filtered out and dried. The yield totaled 45 g, or 83% of the theoretical.

Evaporating the hydrochloric mother liquor yielded a small quantity of a product that proved to be 5-nitro-2-methylbenzimidazole after it was purified.

5,6-Diamino-2-methylbenzimidazole. 30 ml of conc. hydrochloric acid and 20 g of granulated tin were placed in a small flask. Then 10 g of 5,6-dinitro-2-methylbenzimidazole hydrochloride was gradually added portionwise. The addition of each portion was accompanied by a violent reaction and the evolution of considerable heat. After addition was complete, the mass was heated for another 5-10 minutes until the solution had the color of strong tea. It was then decanted from the beaker containing the tin residue, the double tin salt of the reduction product settling out as the solution cooled. The salt was filtered out, squeezed out well to free it of the mother liquor, and dissolved in water, the tin being thrown down by passing a current of hydrogen sulfide through the solution. The mother liquor was evaporated to dryness in an evaporating dish on a water bath. This yielded 7 g of the dihydrochloride of 5,6-diamino-2-methyl-benzimidazole (approximately 80% of the theoretical) as a brownish powder that was excellently soluble in water. The diamine could be recovered from the solution as elongated sand-colored needles by carefully adding ammonia to a conc. aqueous solution of its hydrochloride and rubbing with a glass rod. The free diamine was also rather freely soluble in water, and particularly so in aqueous ammonia and alkalies, though it oxidized with extraordinary ease. This made working with it highly inconvenient.

Condensing 5,6-diamino-2-methylbenzimidazole with organic acids. Condensation was always effected by heating 2.35 g (0.01 mole) of the diamine dihydrochloride with 0.01 mole of the organic acid in 5 ml of 15% hydrochloric acid to 180° in sealed tubes for one hour. The reaction mass was then diluted with water and treated with ammonia, the condensation product being filtered out, washed with water, and then purified.

a) Condensation with formic acid yielded 1.5 g of methyldiimidazolo-1,2,4,5-benzene (VI), or 85% of the theoretical yield. The product was purified by dissolving it in water containing acetic acid, boiling with activated charcoal, and precipitating it from the hot solution with ammonia. M.p. 388-390°. A white, finely acicular product, freely soluble in aqueous mineral acids and acetic acid, sparingly soluble in most solvents. Its hydrochloride can be precipitated from an aqueous solution by acetone or by a large excess of conc. hydrochloric acid.

b) Condensation with acetic acid yielded 1.5 g of dimethyldiimidazolo-1,2,4,5-benzene (VII) – 80% of the theoretical yield. The product was refined like the preceding one. M.p. 438-439°. Its properties resembled those of the preceding compound, but its hydrochloride was salted out from solution by hydrochloric acid somewhat more easily.

c) Condensation with benzoic acid yielded 1.5 g of methylphenyldiimidazolo-1,2,4,5-benzene (VIII) – 60% of the theoretical yield. The product was excellently refined as its hydrochloride, which crystallized from water containing hydrochloric acid as minute white needles.

0.1809 g subs.: 0.1602 AgCl. 0.1107 g subs.: 16.5 ml N_2 (16°, 760 mm). 0.1483 g subs.: 22.2 ml N_2 (20°, 770 mm). Found %: N 17.5, 17.8; Cl 21.92. $C_{15}H_{12}N_4 \cdot 2HCl$. Calculated %: N 17.45; Cl 22.1.

d) Condensation with phenylacetic acid yielded 2 g of methylbenzyldiimidazolo-1,2,4,5-benzene (IX) – approximately 77% of the theoretical yield. The substance was purified by crystallizing its dihydrochloride from water, being secured as minute white needles.

0.1070 g subs.: 14.75 ml N_2 (12°, 760 mm). 0.2212 g subs.: 0.1875 g AgCl. 0.1476 g subs.: 0.1252 g AgCl. Found %: N 16.55; Cl 20.95, 21.18. $C_{16}H_{14}N_4 \cdot 2HCl$. Calculated %: N 16.73; Cl 21.2.

e) Condensation with hydrocinnamic acid yielded 2 g methyl-β-phenylethyldimidazolo-1,2,4,5-benzene (X) – approximately 73% of the theoretical yield. The product was purified as its dihydrochloride, as in the preceding experiment.

0.1294 g subs.: 17.4 ml N_2 (12°, 760 mm). 0.1523 g subs.: 0.1251 g AgCl. 0.1400 g subs.: 0.1145 g AgCl. Found %: N 16.1; Cl 20.3, 20.25. $C_{17}H_{16}N_4 \cdot 2HCl$. Calculated %: N 16.05; Cl 20.35.

f) Condensation with 2-phenylbenzimidazole-5-carboxylic acid yielded 2 g of a derivative of diimidazolo-1,2,4,5-benzene (XI), which was purified from water as a salt containing three molecules of hydrochloric acid. It is very difficult to filter solutions of this salt.

0.1354 g subs.: 19.9 ml N_2 (18°, 773 mm). 0.1530 g subs.: 0.1378 g AgCl.
Found %: N 17.55; Cl 22.3. $C_{22}H_{16}N_6 \cdot 3HCl$. Calculated %: N 17.75; Cl 22.5.

Nitration of benzimidazole. The benzimidazole was nitrated to a 5-nitro derivative, and the latter was recovered as a nitrate after the mass had been poured into water by procedures that were fully analogous to those described for 2-methylbenzimidazole. The nitration product yield was approximately 95% of the theoretical. The second nitro group was added by refluxing 47 g of the nitrobenzimidazole nitrate for two hours in a solution of 94 ml of nitric acid (sp.gr. 1.52) and 49 ml of sulfuric acid (sp.gr. 1.84). Then the mass was poured into 500 ml of water containing ice, and the precipitated nitrate was filtered out. The product was converted into a base by carefully reacting an aqueous solution of the nitrate with ammonia, the base being recrystallized several times from water, yielding needles that fused, though not sharply, at 186°. The yield was 23 g, or 53% of the theoretical. The mother liquors probably contain nothing but a mixture of the initial product and the same dinitro product, since evaporation and numerous crystallizations of these liquors yielded very minute quantities of both of these compounds. The substance with an unsharp m.p. of 186° was analyzed.

0.1078 g subs.: 25.4 ml N_2 (24°, 764 mm). Found %: N 27.2. $C_7H_4N_4O_4$. Calculated %: N 26.9.

5,6-Diaminobenzimidazole. 25 g of granulated tin and 40 ml of conc. sulfuric acid were placed in a small, round-bottomed flask, and 8 g of the dinitro product with a m.p. of 186° was added portionwise. The reaction was very violent. As the resulting solution cooled, the double tin salt settled; it was filtered out and decomposed with hydrogen sulfide, the filtrate being evaporated to dryness on a water bath. This yielded 5.4 g of the diamine dihydrochloride as heavy brown crystals. We were unable to purify the product or convert it into a base because of its extremely high oxidizibility. Determination of the chlorine in the crude product yielded the following results:

0.1025 g subs.: 0.1340 g AgCl. Found %: Cl 32.25. $C_7H_8N_4 \cdot 2HCl$. Calculated %: Cl 32.1.

Condensation of 5,6-diaminobenzimidazole with organic acids. The condensation was always effected with 0.01 moles of the initial substances, as described in the preceding instances.

a) Condensation with formic acid yielded 1.2 g of diimidazolo-1,2,4,5-benzene, or 76% of the theoretical. The product was purified by dissolving it in hot water containing acetic acid, boiling the solution with activated charcoal, and precipitating with ammonia. Minute white needles with a m.p. of approximately 360°, freely soluble in dilute acids and very sparingly soluble in most organic solvents.

b) Condensation with acetic acid yielded 1.2 g of methyldimidazolo-1,2,4,5-benzene (VI), or approximately 70% of the theoretical. The product was purified as in the preceding instance. Its properties and its mixed melting point indicated that it was the same as the product previously prepared from 5,6-diamino-2-methylbenzimidazole and formic acid.

c) Condensation with benzoic acid yielded 1.2 g of phenyldiimidazolo-1,2,4,5-benzene (XV), or approximately 51% of the theoretical. The product was purified as its dihydrochloride, which crystallized satisfactorily from water as white needles.

0.1310 g subs.: 20.5 ml N_2 (20°, 760 mm). 0.1425 g subs.: 0.1335 g AgCl. 0.1913 g subs.: 0.1801 g AgCl.
Found %: N 18.3; Cl 23.19, 23.23. $C_{14}H_{10}N_4 \cdot 2HCl$. Calculated %: N 18.25; Cl 23.35.

d) Condensation with phenylacetic acid yielded 1.7 g of benzyldiimidazolo-1,2,4,5-benzene (XVI), the yield being about 69% of the theoretical. The product was purified as its dihydrochloride by crystallization from water.

0.1010 g subs.: 15 ml N_2 (20°, 770 mm). 0.1159 g subs.: 0.1025 g AgCl. 0.1031 g subs.: 0.0911 g AgCl.
Found %: N 17.53; Cl 21.9, 21.85. $C_{15}H_{12}N_4 \cdot 2HCl$. Calculated %: N 17.45; Cl 22.1.

e) Condensation with β-phenylpropionic acid yielded 1.5 g of β-phenylethyldiimidazolo-1,2,4,5-benzene (XVII). The product was purified as its dihydrochloride by crystallization from water.

0.1073 g subs.: 14.9 ml N_2 (14°, 760 mm). 0.1153 g subs.: 0.099 g AgCl.
Found %: N 16.65; Cl 21.2. $C_{16}H_{14}N_4 \cdot 2HCl$. Calculated %: N 16.73; Cl 21.2.

f) Condensation with 2-phenylbenzimidazole-5-carboxylic acid yielded 1.7 g of the derivative (XVIII), which could be purified by crystallizing the trihydrochloride of that compound from water.

0.1001 g subs.: 15.7 ml N_2 (20°, 764 mm). 0.0609 g subs.: 0.0566 g AgCl.
Found %: N 18.38; Cl 22.97. $C_{21}H_{14}N_6 \cdot 3HCl$. Calculated %: N 18.28; Cl 23.18.

SUMMARY

An investigation of the nitration of benzimidazole derivatives has indicated that this compound cannot be regarded merely as a benzene that contains two substituents in an ortho position to each other. This 2-ring system possesses distinctly specific properties, namely, high reactivity of the 5 and 6 positions and very weak conjugation between these positions. These specific peculiarities of benzimidazole may be attributed to the deformation of the benzene ring caused by the imidazole group condensed with it.

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Received July 22, 1950

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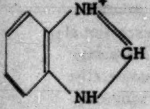
RESEARCH ON IMIDAZOLE DERIVATIVES

IV. THE CHEMICAL PROPERTIES OF DERIVATIVES OF 1,2,4,5-DIIMIDAZOLOBENZENE

L. S. Efros

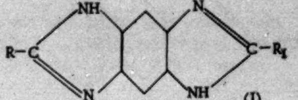
In our preceding report [1] we set forth the hypothesis that the specific peculiarities of benzimidazole and its derivatives, manifested during nitration, are caused by the extensive impairment of the symmetry of the benzene ring in these compounds. This impairment of symmetry, due, most likely, to the attraction of electrons by the imidazole ring, results in the formation of double linkages between the 4-5 and the 6-7 carbon atoms in the benzene ring, while the bond between the 5 and 6 carbon atoms approaches the nature of a single bond (A).



(A)

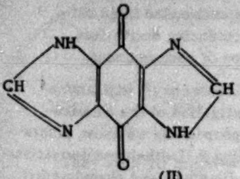
We thought that it would be of interest to make a study of the properties of the derivatives of 1,2,4,5-diimidazolobenzene (I), described previously [1], by way of obtaining further confirmation of the existence of this deformation of the benzene ring.

In a symmetrical molecule of these compounds the effect of two imidazole groups upon the double bonds of the central benzene ring ought to produce considerable unsaturation at the 3 and 6 positions, so that the state of the central benzene ring in Type (I) compounds ought to resemble that of anthracene, while the 3 and 6 positions ought to be like the meso position of the latter.



(I)

The most characteristic property of anthracene and its derivatives is the ability of these compounds to be oxidized to the corresponding anthraquinones fairly easily; we therefore commenced our research with an investigation of derivatives of diimidazolobenzene (I). We found that these compounds actually are oxidized fairly smoothly by a chromic acid mixture, resulting in nearly quantitative yields of the respective derivatives of 1,2,4,5-diimidazolo-3,6-benzoquinone. Thus, by oxidizing unsubstituted 1,2,4,5-diimidazolobenzene with chromic acid in boiling 45-50% sulfuric acid we secured a very high yield of the corresponding quinone (II), the disulfate of which settled out of the reaction mass as well-formed lemon-yellow needles.



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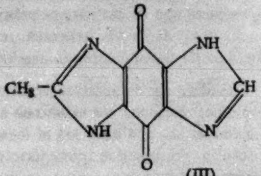

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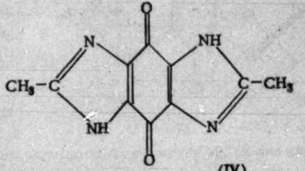
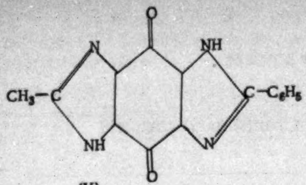


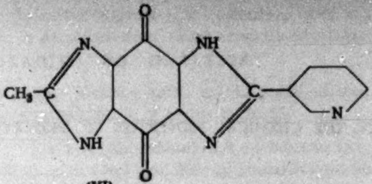
(IV)

Similarly, oxidizing the methyl and dimethyl derivatives of diimidazolobenzene yielded the sulfates of the corresponding quinones (III) and (IV), the properties of which were very much like those of the quinone (II), the only difference being their somewhat lower solubility in acids.

Compounds of similar structure were also readily synthesized by oxidizing the methylphenyl (V) and methyl-β-pyridyl (VI) derivatives of diimidazolobenzene: (see top of next page)

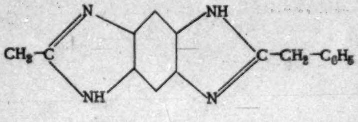
Oxidation of methylbenzyldiimidazolobenzene (VII) was somewhat more difficult, the methylene group in the side chain being likewise oxidized, to judge by the high consumption of the oxidant and the elementary composition of the end product, the resulting compound probably having the composition of (VIII).

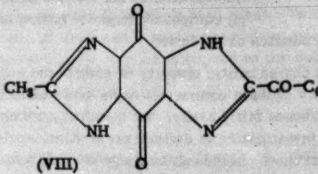

(V)

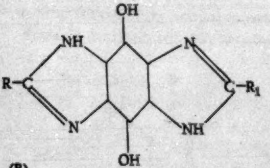

(VI)

The sulfates or dihydrochlorides of all these compounds are lemon-yellow and are asymmetrical, their color being somewhat deeper than that of symmetrical substituted derivatives. As might have been expected, the basicity of the imidazole groups in these compounds is very greatly weakened by the proximity of the carbonyl groups, the sulfates and hydrochlorides referred to above being hydrolyzed even by traces of moisture, as in 96% alcohol. At first we get bright-red monoacid salts, one of which, constituting the compound (V), we managed to isolate in the chemically pure state. Further hydrolysis converts these salts into free quinone bases. In the case of the compounds (II), (III), (IV), and (VIII) these bases are various shades of orange-yellow, the asymmetrical compounds (V) and (VI) being colored violet-red and red respectively.

All these quinones dissolve in aqueous solutions of caustic alkalies, producing violet-blue solutions, from which the alkaline salts of the respective derivatives can be crystallized out by adding an excess of alkali, though mere chilling suffices in the case of the compound (V). We succeeded in purifying the potassium salt of the compound (V) by crystallizing it from water; it was converted thereby into a monometallic salt, probably due to partial hydrolysis, consisting of lustrous dark-green needles. When alkaline solutions of the quinones are reacted with hydrosulfite, they are decolorized as the result of the formation of leuco compounds, with the probable structure of (B).


(VII)


(VIII)


(B)

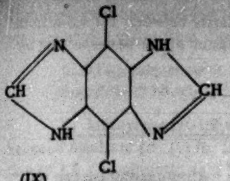
These colorless solutions are readily oxidized by atmospheric oxygen, their original violet-blue color being restored.

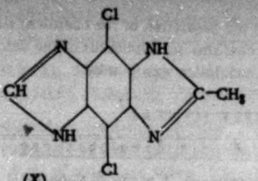
All the foregoing compels us to conclude that 1,2,4,5-diimidazolobenzene and its derivatives behave like anthracene in an oxidation reaction, as we had expected, readily producing derivatives of diimidazolobenzoquinone, an unusual analog of anthraquinone.

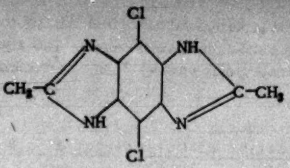
Extending our comparison of diimidazolobenzene (I) with anthracene to other reactions, we undertook an investigation of the chlorination, bromination, and nitration of these compounds. As we know, anthracene can be chlorinated and brominated very readily, the reaction immediately yielding 9,10-dihalogen derivatives [2]. We readily succeeded in chlorinating diimidazolobenzene as well as its methyl, dimethyl, and phenylmethyl derivatives by passing chlorine through solutions of these compounds in dilute hydrochloric acid in the cold. The chlorination products, the dichloro derivatives (IX), (X), (XI), and (XII), which were much less soluble in water, were crystallized from the solution as hydrochlorides: (see top of next page).

The location of the chlorine atoms in these compounds was established by oxidizing these substances with a chromic acid mixture. Chlorine was split out quantitatively in every instance, yielding the previously described quinones (II), (III), (IV), and (V). This transformation of the chloro derivatives upon oxidation indicates how extraordinarily closely these substances are related to anthracene, since such reactions are highly typical of the latter [3].

The introduction of chlorine atoms into diimidazolobenzene derivatives greatly diminishes the basicity of these compounds. The dihydrochlorides of the substances (IX), (X), and (XI), which are freely soluble in cold water,


(IX)


(X)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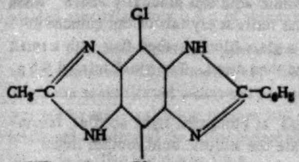
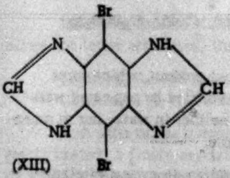
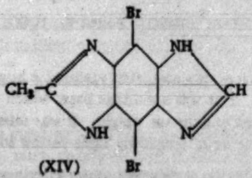

(XII)

hydrolyze when heated, the respective bases settling out. As for the compound (XII), only its monoacid salt is stable.

The derivatives of diimidazolobenzene are likewise readily brominated when they are agitated with bromine in an aqueous 3% sulfuric acid solution. The bromo derivatives settle out, being purified later by crystallization from dilute hydrochloric acid. This yielded the following derivatives:


(XIII)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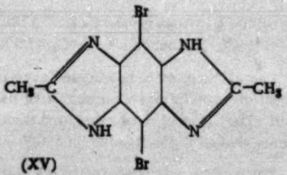
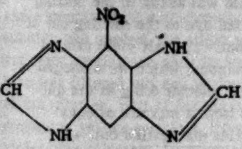
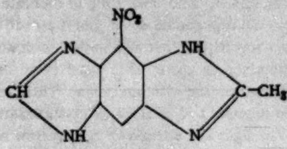
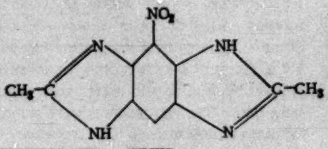

(XV)

Here, too, the position of the bromine atoms was established by oxidizing these substances to convert them into the quinones (II), (III), and (IV) that contained no halogen. The properties of the bromo derivatives greatly resembled those of the chloro substitution derivatives already described, so that we shall not dwell upon them at this point.

The derivatives of diimidazolobenzene (I) are readily nitrated in sulfuric acid under the usual conditions. We were able to isolate the nitro derivatives by pouring the nitro mass into water, carefully neutralizing with ammonia, and then crystallizing from alcohol. This yielded nitro derivatives with the following structures:


(XVI)


(XVII)


(XVIII)

They were all bright-yellow substances that dissolved in dilute mineral acids, producing colorless solutions. The effect of the nitro group increases the acidic properties of the imino groups in these compounds, so that they are fairly freely soluble in ammonia and soda, in addition to caustic alkalies, thus differing from the initial products.

Since we know that anthracene and some of its derivatives can also yield meso dinitro derivatives [4] under certain conditions, we tried to introduce another nitro group into the synthesized substances, but we did not succeed, even when using the most severe conditions. This evidently means that the effect of the nitro group, which prevents the second substituent from entering at the para position, is much stronger in derivatives of diimidazolobenzene than in anthracene.

It is apparently this same circumstance that is responsible for the fact that our attempt to oxidize the nitro compounds into the previously described quinones likewise met with failure. No reaction took place; we recovered the original products unchanged in very case.

The experimental data cited indicate that our prediction of the chemical similarity between 1,2,4,5-diimidazobenzene and anthracene is correct. This also confirms our hypothesis of the deformation of the benzene ring by the imidazole group, upon which this theoretical conclusion was founded.

EXPERIMENTAL

I. Oxidation of Derivatives of 1,2,4,5-Diimidazolobenzene

a) Dimethyl-1,2,4,5-diimidazolo-3,6-benzoquinone. 5 grams of dimethyl-1,2,4,5-diimidazolobenzene was dissolved in 70 ml of 40% sulfuric acid and heated to boiling, and 7.5 g of chromic acid was gradually added. When the reaction was over (it did not set in at once, but later was fairly violent), the lustrous crystals of the quinone disulfate began to settle out of the still hot solution. They were filtered out on a glass filter, washed first with a small amount of cold 40% sulfuric acid and then with absolute alcohol and ether, and then dried. The yield totaled 9.5 g of beautiful light-yellow crystals.

The quinone sulfate could be readily crystallized from 40% sulfuric acid, as elongated light needles, lemon-yellow in color, which were washed with absolute alcohol and ether to eliminate the sulfuric acid mother liquor (aqueous alcohol hydrolyzed the salt). The percentage of sulfuric acid in the salt was determined by analysis, a sample being dissolved in water containing hydrochloric acid and the $SO_4^=$ precipitated with barium chloride.

0.1030 g, 0.1045 g substance: 0.1168 g, 1.1181 g $BaSO_4$. Found %: H_2SO_4 47.56, 47.45. $C_{10}H_8O_2N_4 \cdot$ $\cdot 2H_2SO_4$. Calculated %: H_2SO_4 47.57.

The quinone salt is hydrolyzed even by traces of water, first yielding a bright-red product, which turns orange-yellow upon further treatment with water. This was a quinone base, which was purified by repeated washings with water, alcohol, and ether, and then dried to constant weight. It was soluble neither in water nor in organic solvents, though it did dissolve in 5-10% sulfuric acid, producing light-yellow solutions.

The quinone was also soluble in caustic alkalies, producing violet solutions. Adding an excess of alkali decolorized the solution, the quinone salts crystallizing out as dark needles. Alkaline solutions of the quinone were decolorized when hydrosulfite was added. When the solution was shaken up with air, the color reappeared. The melting point of the base lay above 400°.

0.1055 g substance: 0.2130 g CO_2, 0.0371 g H_2O. 0.1440 g, 0.1069 g substance: 32.6 ml, 24.2 ml N_2 (22°, 752 mm). Found %: C 55.4; H 3.9; N 25.92, 25.91. $C_{10}H_8O_2N_4$. Calculated %: C 55.5; H 3.7; N 25.92.

b) Methyl-1,2,4,5-diimidazolo-3,6-benzoquinone. 1.2 grams of methyl-1,2,4,5-diimidazolobenzene (cf [1] for its synthesis) was dissolved in 15 ml of 40% sulfuric acid, and 1.8 g of chromic acid was added to the boiling solution. When the reaction was over and the solution cooled down, the mass solidified due to the settling out of crystals of the quinone disulfate. The product was filtered out and washed with alcohol. The salt yield totaled 1.2 g. In this case the mother liquor still contained an appreciable quantity of the quinone, which we managed to recover by diluting with water and carefully neutralizing with ammonia. This yielded another 0.5 g of the quinone base. The two products were combined together and purified by crystallization from a mixture of equal volumes of 40% sulfuric acid and alcohol. The light and elongated light-yellow needles that settled out, were washed with absolute alcohol and ether and dried, as in the preceding experiment. The percentage of sulfuric acid in the quinone salt was determined by analysis, as in the preceding test.

0.1003 g substance: 0.1175 g $BaSO_4$. Found %: H_2SO_4 49.20. $C_9H_6O_2N_4 \cdot 2H_2SO_4$. Calculated %: H_2SO_4 49.24.

The quinone base was obtained by boiling the recrystallized salt with water, the orange-yellow precipitate being filtered, washed with water, alcohol, and ether, and dried to constant weight. The quinone did not melt when heated to 400°. It was insoluble in organic solvents, though it did dissolve in aqueous caustic alkalies, producing violet-blue solutions that were decolorized by hydrosulfite.

0.1026 g substance: 25.5 ml N_2 (24°, 740 mm). Found %: N 27.81. $C_9H_6O_2N_4$. Calculated %: N 27.72.

c) 1,2,4,5-Diimidazolo-3,6-benzoquinone. This was prepared exactly like the quinones described above. In this case, however, it is best to isolate it from the reaction mass as a base, owing to the high solubility of its sulfate in water. This was done by diluting the reaction mass with water and partially neutralizing it with ammonia. The precipitated base was filtered out and washed well with water, alcohol, and ether. One gram of diimidazolobenzene yielded approximately 1 g of the quinone base. The color, solubility, and properties of this product hardly differ from those of the compounds described previously.

0.1012 g substance: 0.1892 g CO_2, 0.0201 g H_2O. 0.1297 g substance: 33.6 ml N_2 (22°, 752 mm). Found %: C 50.93; H 2.20; N 29.66. $C_8H_4O_2N_4$. Calculated %: C 51.06; H 2.13; N 29.79.

d) Methylphenyl-1,2,4,5-diimidazolo-3,6-benzoquinone. 2.6 grams of methylphenyl-1,2,4,5-diimidazolobenzene disulfate (cf. [1] for its synthesis) was dissolved by heating it in 60 ml of 50-60% sulfuric acid, and a solution of 1.5 g of chromic acid in 2-3 ml of water was added. Chilling resulted in crystallizing out a minute quantity of the sulfate of the original product, which was filtered out and converted into the hydrochloride [1]. This yielded approximately 0.5 g of this salt.

The green mother liquor was diluted with 4 times its volume of water, which caused it to turn red. It was neutralized with ammonia and then with sodium acetate until it no longer reacted acid with Congo red, after which the precipitated violet-red reaction product was filtered out and washed well with water. The product was purified by recrystallizing it from 200 ml of dilute hydrochloric acid, from which it was recovered as well-formed, bright-red needles of the monohydrochloride. They were thoroughly washed with absolute alcohol and ether, and then dried. The yield was 1.5 g.

0.1024 g substance: 0.0482 g AgCl. Found %: Cl 11.65. $C_{15}H_{10}O_2N_4 \cdot HCl$. Calculated %: Cl 11.29.

When the mother liquor, which contained hydrochloric acid, was not washed out of the monohydrochloride before the latter was dried, the salt gradually turned into the light-yellow sulfate. The latter salt was also analyzed.

0.1359 g, 0.1366 g substance: 0.1128 g, 0.1131 g AgCl. Found %: Cl 20.5, 20.5 $C_{15}H_{10}O_2N_4 \cdot 2HCl$. Calculated %: Cl 20.25.

Both salts of the quinone in question were somewhat soluble in cold water, but they hydrolyzed when only gently heated, a finely crystalline, more deeply colored quinone base settling out. It was filtered out, washed with water, alcohol, and ether, and then dried to constant weight.

0.1045 g substance: 0.2475 g CO_2, 0.0341 g H_2O. 0.1187 g substance: 20.8 ml N_2 (22°, 752 mm). Found %: C 64.5; H 3.62; N 20.07. $C_{15}H_{10}O_2N_4$. Calculated %: C 64.75; H 3.59; N 20.17.

The quinone base dissolved in caustic alkalies, producing a violet color; when these solutions were cooled, they were decolorized, the quinone salt crystallizing out in beautiful needles. This salt could be recrystallized from water, being obtained as large green needles.

e) Methyl-β-pyridyl-1,2,4,5-diimidazolo-3,6-benzoquinone. 1.7 grams of methyl-β-pyridyl-1,2,4,5-diimidazolobenzene was dissolved in 15 ml of concentrated sulfuric acid, the solution was diluted with 30 ml of water, and a solution of 3 g of chromic acid in 5 ml of water was added. When the vigorous reaction was over and the solution had cooled, the slight precipitate was filtered out, the solution being diluted with water to make 200 ml and then neutralized until its reaction was rather rigorously neutral. The resulting red precipitate of the quinone base was filtered out and washed with water, alcohol, and ether. The yield totaled 0.7 g (judging by the red color of the solution, part of the product was lost in the mother liquor). The product dissolved readily in dilute acids, producing yellow solutions, from which no quinone salt could be isolated. Heating in aqueous alkalies produced violet-blue solutions, from which a crystalline precipitate settled out upon cooling, the solutions being decolorized.

0.1032 g substance: 22.2 ml N_2 (15°, 750 mm). Found %: N 25.17. $C_{14}H_9O_2N_5$. Calculated %: N 25.09.

II. Chlorination and Bromination of 1,2,4,5-Dimidazolobenzene Derivatives

One gram of 1,2,4,5-diimidazolobenzene or of one of its derivatives was always dissolved in 50 ml of dilute hydrochloric acid, and gaseous chlorine was passed through the resultant solutions. White precipitates of the respective dichloro derivatives gradually separated as hydrochlorides. They were filtered out and crystallized several times from water containing hydrochloric acid.

a) The yield of 3,6-dichloro-1,2,4,5-diimidazolobenzene dihydrochloride totaled 1.5 g. White crystals, soluble in cold water and settling out when these solutions were heated, owing to hydrolysis. Adding hydrochloric acid produces dissolution, while an excess of the hydrochloric acid salts the substance out of the solution.

Determining the ionizing chlorine: 0.1012 g, 0.1015 g substance: 0.0971 g, 0.0973 g AgCl. Found %: Cl 23.70, 23.68. $C_8H_4N_4Cl_2 \cdot 2HCl$. Calculated %: Cl 23.67.

Determining total chlorine: 0.1025 g, 0.1073 g substance: 0.1960 g, 0.2055 g AgCl (Carius). Found %: Cl 47.28, 47.25. $C_8H_6N_4Cl_4$. Calculated %: Cl 47.33.

b) The yield of methyl-3,6-dichloro-1,2,4,5-diimidazolobenzene hydrochloride was 1.5 g. It differed from the preceding product only in its poor solubility in water and particularly in dilute hydrochloric acid.

Determining the ionizing chlorine: 0.1100 g substance: 0.0997 g AgCl. Found %: Cl 22.4. $C_9H_6N_4Cl_2 \cdot 2HCl$. Calculated %: Cl 22.6.

c) Dimethyl-3,6-dichloro-1,2,4,5-diimidazolobenzene dihydrochloride. 1.4 g yield. It differed from the preceding compounds only in its somewhat poorer solubility.

Determining the ionizing chlorine: 0.1068 g, 0.1157 g substance: 0.0935 g, 0.1005 g AgCl. Found %: Cl 21.67, 21.5. $C_{10}H_8N_4Cl_2 \cdot 2HCl$. Calculated %: Cl 21.65

Determining the total chlorine: 0.1027 g, 0.1003 g substance: 0.1822 g, 0.1773 g AgCl (Carius). Found %: Cl 43.71, 43.7. $C_{10}H_{10}N_4Cl_4$. Calculated %: Cl 43.29.

Part of the product was converted into a base by treating it with aqueous ammonia, the base being thoroughly washed with water and dried before analysis.

0.1004 g, 0.1001 g substance: 0.1119 g, 0.1110 g AgCl. Found %: Cl 27.55, 27.45. $C_{10}H_8N_4Cl_2$. Calculated %: Cl 27.85.

d) Methylphenyl-3,6-dichloro-1,2,4,5-diimidazolobenzene hydrochloride. 1.1 g yield. The product dissolved with difficulty in water, slightly acidulated with hydrochloric acid, and differed from the preceding compounds in precipitating monohydrochloride.

Determining the ionizing chlorine: 0.0906 g substance: 0.0367 g AgCl. Found %: Cl 10.03. $C_{15}H_{10}N_4Cl_2 \cdot HCl$. Calculated %: Cl 10.3.

Determining the total chlorine: 0.1055 g substance: 0.1279 g AgCl (Carius). Found %: Cl 30.01. $C_{15}H_{11}N_4Cl_3$. Calculated %: Cl 30.13.

2) All the derivatives of diimidazolobenzene were brominated as follows: 0.005 mole of the original compound was dissolved in 50 ml of water, to which the necessary quantity of sulfuric acid was added. 1.6 grams of bromine was added to the resulting solution, and the whole was agitated vigorously. The bromination product soon settled out; it was filtered out and crystallized from water containing hydrochloric acid.

a) 3,6-Dibromo-1,2,4,5-diimidazolobenzene dihydrochloride.

Determining the ionizing chlorine: 0.1015 g, 0.1026 g substance: 0.0747 g, 0.0755 g AgCl. Found %: Cl 18.20, 18.25. $C_8H_4N_4Br_2 \cdot 2HCl$. Calculated %: Cl 18.25.

Treating the product with aqueous ammonia converted it into a base, which was thoroughly washed with water and dried, after which it was analyzed.

0.1002 g, 0.1076 g substance: 0.1189 g, 0.1279 g AgBr. Found %: Br 50.65, 50.67. $C_8H_4N_4Br_2$. Calculated %: Br 50.63.

b) Methyl-3,6-dibromo-1,2,4,5-diimidazolobenzene dihydrochloride.

0.1007 g, 0.1101 g substance: 0.0716 g, 0.0782 g AgCl. Found %: Cl 17.58, 17.6. $C_9H_6N_4Br_2 \cdot 2HCl$. Calculated %: Cl 17.61.

The bromine in the free base was determined by the Carius method:

0.0987 g, 0.0951 g substance: 0.1120 g, 0.1081 g AgBr. Found %: Br 48.3, 48.45. $C_9H_6N_4Br_2$. Calculated %: Br 48.48.

c) Dimethyl-3,6-dibromo-1,2,4,5-diimidazolobenzene dihyrochlor ide.

0.0990 g, 0.0984 g substance: 0.0686 g, 0.0680 g AgCl. Found %: Cl 17.09, 17.07. $C_{10}H_8N_4Br_2 \cdot 2HCl$. Calculated %: Cl 17.05.

The bromine in the free base was determined by the Carius method:

0.1087, 0.1008 g substance: 0.1201 g, 0.1101 g AgBr. Found %: Br 47.0, 46.45.
$C_{10}H_8N_4Br_2$. Calculated %: Br 46.51.

3) The chloro and bromo derivatives were oxidized and the quinones were isolated by about the same methods as those described in detail in Part (1) of the experimental section. The quinones synthesized from the halogen derivatives were identified with those synthesized previously by their properties and qualitative reactions. Moreover, we checked the absence of halogen in these compounds by a Beilstein test in every case. All of these tests were negative. The oxidation of the dibromo derivative of dimethyldiimidazolobenzene is described below by way of example.

0.6 gram of the dibromide was dissolved in 10 ml of concentrated sulfuric acid and then diluted with 15 ml of water. 0.5 gram of chromic acid was added to the solution, which was then heated to boiling. The odor of the liberated bromine became clearly perceptible and the oxidation reaction proceeded. As the solution cooled the quinone sulfate settled out; it was purified as described above (see Ia). It contained no halogen, and its properties indicated its identity with the compound (IV) described previously.

III. Nitration of Diimidazolobenzene Derivatives.

0.01 gram of the original diimidazolobenzene derivative was dissolved in 12 ml conc. sulfuric acid and a nitrating mixture of 0.5 ml of nitric acid (sp.gr. 1.48) and 1 ml of sulfuric acid was added a drop at a time at 15-20°, with mechanical stirring. After the mass had stood for half an hour, it was poured into 100 ml of water and carefully neutralized with ammonia. Bright-yellow products settled out; they were filtered out, thoroughly washed with water, and dried, after which it was crystallized from alcohol. The product yields approached the quantitative.

The synthesized substances were only very slightly soluble in water, freely soluble in aqueous solutions of mineral acids, producing colorless solutions, somewhat less soluble in acetic acid, freely soluble in caustic alkalies, and moderately soluble in ammonia. They settled out of solution as yellow needles at their isoelectric point. The melting point of the products lay above 360°.

a) Nitrodiimidazolobenzene (XVI).

0.0105 g substance: 29.3 ml N_2 (15°, 760 mm). 0.0955 g substance: 28.0 ml N_2 (16°, 760 mm).
Found %: N 34.60, 34.65. $C_8H_5O_2N_5$. Calculated %: N 34.48.

b) Nitromethyldiimidazolobenzene (XVII).

0.0982 g substance: 26.4 ml N_2 (16°, 770 mm) 0.0809 g substance: 22.1 ml N_2 (17°, 770 mm).
Found %: N 32.20, 32.55. $C_9H_7O_2N_5$. Calculated %: N 32.26.

c) Nitrodimethyldiimidazolobenzene (XVIII).

0.1175 g substance: 30.3 ml N_2 (24°, 774 mm). Found %: N 30.28. $C_{10}H_9O_2N_5$. Calculated %: N 30.30.

We attempted to nitrate these compounds further under varying conditions, but without success. For instance, 4 g of the nitro product (XVIII) was refluxed in a solution of 4 ml of concentrated sulfuric acid and 8 ml of nitric acid (sp. gr. 1.5) for three hours. The mass was poured into water and neutralized with ammonia. A yellow product settled out, which was filtered out and purified, proving to be the original compound. Refining yielded 3.5 g of the substance.

We attempted to oxidize these compounds by boiling them with a chromic acid mixture the sulfuric acid in which was raised as high as 70%. The oxidant was gradually consumed [1.5 g of chromic anhydride being taken per gram of the nitro product (XVIII)], but still the product was recovered unchanged.

SUMMARY

The hypothesis advanced in our preceding report [1] that the benzene ring is deformed by benzimidazole derivatives enabled us to draw the theoretical conclusion that 1,2,4,5-diimidazolobenzene and anthracene were chemically similar in the constitution of their central benzene rings. This conclusion has been confirmed by our experimental investigation of the chemical properties of diimidazolobenzene derivatives. In our research we have secured new derivatives of 1,2,4,5-diimidazolobenzene, as well as chloro, bromo, and nitro derivatives of 1,2,4,5-diimidazolobenzene.

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Received July 22, 1950

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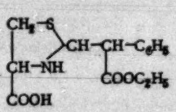
THIAZOLIDINE-4-CARBOXYLIC ACID AND ITS DERIVATIVES

II. S-SUBSTITUTION DERIVATIVES OF CYSTEINE AND THEIR TRANSFORMATION INTO DERIVATIVES OF THIAZOLIDINE-4-CARBOXYLIC ACID

I. T. Strukov

In Report I we showed [1] that it is fairly easy to close the pyrrolidine ring, producing thiazolidine-pyrrolidine ring systems.

In the present research we endeavored to use this method to secure simple model compounds with a thiazolidine-β-lactam ring system by synthesizing 2-(α-phenyl-α-carbethoxymethyl)-thiazolidine-4-carboxylic acid [1] from l-cysteine hydrochloride and ethyl formylphenylacetate (II) [2].

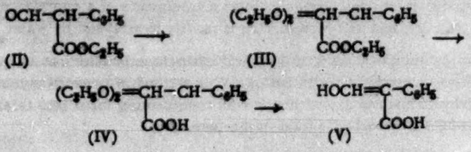


(I)

We were unable to close the β-lactam ring, however: no reaction took place when the compound (I) was heated to 100°, while carbon dioxide and hydrogen sulfide were given off at 150-160°. It was apparent that the foregoing method could not be employed in this instance. The same result was secured when 2-(α-phenyl-α-carbethoxymethyl)-thiazolidine-4-carboxylic acid was used. We therefore tried to saponify the ester group in (I) and then close the β-lactam ring. We found that saponifying it in an aqueous alcoholic solution with sodium hydroxide under mild conditions simultaneously ruptured the thiazolidine ring.

Preparation of 2-(α-phenyl-α-carboxymethyl)-thiazolidine-4-carboxylic acid (VII) by another method required formylphenylacetic acid (V), which we thought we could produce from its ester, but when we saponified ethyl formylphenylacetate under relatively mild conditions we got phenylacetic acid rather than formylphenylacetic acid. The formyl group proved to be unstable in the presence of an aqueous-alcoholic alkali.

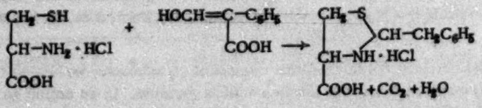
We managed to prepare formylphenylacetic acid from ethyl formylphenylacetate, however, via the diethyl acetal of ethyl formylphenylacetate (III) and the diethyl acetal of formylphenylacetic acid (IV), by treating the latter with concentrated hydrochloric acid:



(II) (III) (IV) (V)

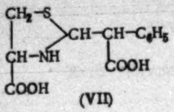
It was synthesized in the oxymethylene form. Oxymethylenephenylacetic acid is fairly stable in an acid medium, but is readily decomposed by an alkali, yielding phenylacetic acid.

When oxymethylenephenylacetic acid is condensed with l-cysteine hydrochloride in methanol at room temperature, carbon dioxide is liberated and 2-benzylthiazolidine-4-carboxylic acid (VI) is produced, which readily hydrolyzes in water:



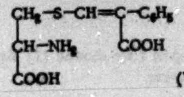
(VI)

The same results were obtained when this reaction was carried out in pyridine. It was found that pyridine breaks down oxymethylenephenylacetic acid very rapidly, forming phenylacetaldehyde and carbon dioxide. Hence, the cysteine reacts with the phenylacetaldehyde rather than with the oxymethylenephenylacetic acid, giving rise to the compound (VI). Only once were we able to prepare 2-(α-phenyl-α-carboxymethyl)-thiazolidine-4-carboxylic acid (VII): by condensing the diethyl acetal of formylphenylacetic acid with l-cysteine hydrochloride.


(VII)

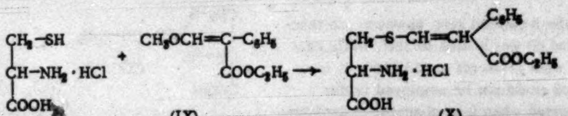
All attempts to repeat that experiment were unsuccessful, 2-benzylthiazolidine-4-carboxylic acid being secured every time.

Inasmuch as oxymethylenephenylacetic acid is fairly stable in an acid medium, we tried to condense it with dl-cysteine in concentrated hydrochloric acid at 0°. This yielded S-β-(α-phenyl-α-carboxy)-ethylenecysteine hydrochloride instead of the thiazolidine compound (VII); we isolated the free acid (VIII) from this hydrochloride.


(VIII)

Concentrated hydrochloric acid apparently blocks the primary amino group, which does not take part in the reaction.

The reaction followed the same lines when ethyl formylphenylacetate and ethyl methoxymethylenephenylacetate (IX) were condensed with dl-cysteine. In both cases we secured the hydrochloride of S-β-(α-phenyl-α-carbethoxy)-ethylenecysteine (X), from which we isolated the free acid (XI):


(IX) (X)

Ethyl formylphenylacetate exists in three tautomeric forms [3], though only the oxymethylene form can yield the compound (X). Hence the yield when ethyl methoxymethylenephenylacetate was used was about twice as high as when we used ethyl formylphenylacetate.

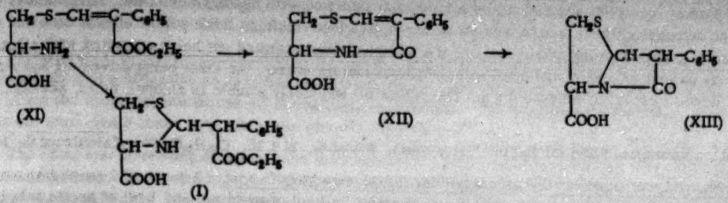
The S-substitution derivatives of cysteine, in which the sulfur is linked to a carbon atom that has a double bond, may be regarded as a tautomeric form of thiazolidine compounds, though we know of no instances of a conversion of thiazolidine compounds into S-substituted compounds. The physical and chemical properties of the S-substitution derivatives of cysteine differ greatly from those of the corresponding thiazolidine compounds: they are not oxidized by an iodine solution, they do not react with mercuric chloride in the cold, they form freely water-soluble salts with mineral acids, and their acetyl compounds have low melting points. The thiazolidine compounds described by Ratner and Clarke [4] and other authors behave differently. Compound (I), in particular, is oxidized by iodine and reacts with mercuric chloride to form a precipitate of a complex mercuric salt of cysteine and the formylphenylacetic ester, and its hydrochloride is readily hydrolyzed by water.

It is worthy of note that the aldehydic form of the formylphenylacetic ester can be secured in the pure state by oxidizing the thiazolidine compound (I) with iodine. This method of converting compounds that have two tautomeric forms – the aldehydic and the oxymethlenic – by transforming them into thiazolidine compounds may make it possible to isolate only the aldehydic form in the pure state.

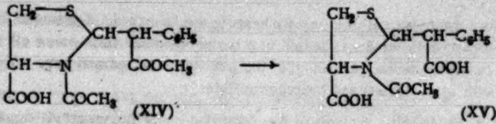
In connection with the synthesis of S-substitution derivatives of cysteine the idea arose of trying to convert the compound (XI) into a compound with a seven-membered ring system (XII), in the expectation that a further shift of hydrogen from the nitrogen atom to the double bond would take place, yielding the thiazolidine-β-lactam ring system (XIII): (see top of next page).

According to Fisher [5] six-membered ring systems may be closed rather readily in an intramolecular reaction of the methyl esters of Δ-amino acids. Though closing the seven-membered rings of esters of ε-amino acids is much more difficult, testing this hypothesis was of extraordinary interest in solving problems involved in the synthesis of penicillin.

As a matter of fact, we obtained the thiazolidine compound (I) whenever we heated the sodium salt of S-β-(α-phenyl-α-carboethoxy)-ethylenecysteine or the free acid in pyridine. In an amino group that is not linked to hydrogen chloride, therefore, the hydrogen resumes its mobility and shifts to the double bond, resulting in closure of the thiazolidine ring. The same holds true of the carbomethoxy analog as in the compound (VIII), no thiazolidine compound is formed. Ratner and Clarke consider thiazolidine compounds to be in a state of equilibrium with cysteine and the aldehyde.


(XI) (I) (XII) (XIII)

When thiazolidine compounds are acylated, the bonds between the sulfur and nitrogen atoms and the carbon atoms are stabilized, and the sulfur is not oxidized by iodine. We were able to saponify the acetyl compound (XIV) produced by acetylating 2-(α-phenyl-α-carbomethoxymethyl)-thiazolidine-4-carboxylic acid (I), obtaining 2-(α-phenyl-α-carboxymethyl-N-acetylthiazolidine-4-carboxylic acid (XV):


(XIV) (XV)

Stabilization of thiazolidine compounds by acylating an amino group is an extremely interesting problem in theoretical chemistry. It is hard to judge the strength or the stability of the bonds in most organic molecules. When we compare the compounds (XI) and (XIV), we can hardly say that the bond between the sulfur and the carbon atom in the ethylene group in (XI) is more stable than in the compound (XIV). But when thiazolidine compounds are acylated, the energy expended in binding the nitrogen atom to the CH_3CO group is taken from the nitrogen, thus reinforcing the bond between the sulfur and carbon atoms in the compound (XIV).

As for the instability of oxymethylenephenylacetic acid, it must be assumed that it is related to the mobility of the hydrogen in the oxymethylene group, which results in this compound's existing in several tautomeric forms. This also gives rise to the differing nature of its cleavage: it is converted into phenylacetic acid by the action of an alkali, while dissolution in pyridine converts it into phenylacetaldehyde and carbon dioxide.

EXPERIMENTAL

2-(α-Phenyl-α-carbethoxymethyl)-thiazolidine-4-carboxylic acid. 10 grams of l-cysteine hydrochloride, 12 g of ethyl formylphenylacetate, and 2 ml of water were placed in a 50-ml round-bottomed flask and heated and stirred for 15 minutes on a boiling water bath, producing a transparent, light-yellow solution. The solution was gradually poured into 250 ml of water, and 46 ml of an 8% solution of sodium bicarbonate was slowly added. The next day the precipitate was filtered out, washed with water, and dried in a vacuum desiccator. Then it was washed with ether and recrystallized from alcohol. Very thin needles with an m.p. of 168-169° (with decomposition).

8.239 mg substance: 0.337 ml N_2 (21.5°, 757 mm). 7.735 mg substance: 0.308 ml N_2 (19°, 758 mm). Found %: N 4.64, 4.71. $C_{14}H_{17}O_4NS$. Calculated %: N 4.74.

The hydrochloride of the 2-(α-phenyl-α-carbethoxymethyl)-thiazolidine-4-carboxylic acid was prepared by passing anhydrous hydrogen chloride through an ether solution of the acid; m.p. 163-165° (with decomposition). 2 grams of the acid was dissolved in 20 ml of water, a solution of sodium bicarbonate was gradually added, and the solution was treated with an 0.1N solution of iodine until the light-yellow coloring persisted for several seconds. The solution was treated with three times its weight of ether, the ether extract was dried with sodium sulfate, the ether was driven off, and the residual oil was distilled in vacuo. B.p. 135-140° at 10 mm. The oil crystallized, the crystals being washed with gasoline. This yielded flakes with an m.p. of 70-71°, which exhibited a silver mirror reaction. They were identified as the keto form of ethyl formylphenylacetate, synthesized by Wislicenus [2].

After the ether extraction l-cysteine was recovered from the aqueous solution as regular hexagonal crystals.

Methyl ester of 2-(α-phenyl-α-carbethoxymethyl)-thiazolidine-4-carboxylic acid. 5 grams of the acid was dissolved in 50 ml of methanol, and the chilled solution was saturated with hydrogen chloride. The next day the solvent and the hydrogen chloride were driven off in vacuo, and the remaining thick yellow oil was dissolved in water, the resulting solution being alkalinized and the substance that separated out being extracted with ether. The extract was washed with water and dried with anhydrous sodium sulfate, the ether being driven off and the residual oil being dried in vacuo. It weighed 4.7 g. The yellow oil was freely soluble in alcohol, ether, acetone, and benzene.

7.299 mg substance: 0.285 ml N_2 (19°, 741.4 mm). Found %: N 4.45. $C_{15}H_{19}O_4NS$. Calculated %: N 4.53.

2-(α-Phenyl-α-carbethoxymethyl)-N-acetylthiazolidine-4-carboxylic acid. 2 grams of 2-(α-phenyl-α-carbethoxymethyl)-thiazolidine-4-carboxylic acid was dissolved in 5 ml of pyridine, and 1 ml of acetic anhydride was added. One hour later the mass was gradually poured into 20 ml of 20% sulfuric acid. The resulting precipitate was filtered out, washed with water, dried, and recrystallized from methanol; m.p. 209-211°. The substance was freely soluble in methanol, ether, and acetone, less so in benzene.

7.467 mg substance: 0.284 ml N_2 (20.5°, 723 mm). Found %: N 4.20. $C_{16}H_{19}O_5NS$. Calculated %: N 4.15.

Attempt to close the β-lactam ring. a) By heating the free acid. 4 grams of 2-(α-phenyl-α-carbethoxymethyl)-thiazolidine-4-carboxylic acid was heated in a round-bottomed flask on an oil bath to 100-120° for 6 hours. No changes occurred in the substance. At 150-160° the substance melted and gave off carbon dioxide (precipitate of barium carbonate with baryta water) and hydrogen sulfide.

b) Heating the sodium salt. 4 grams of 2-(α-Phenyl-α-carbethoxymethyl)-thiazolidine-4-carboxylic acid was dissolved in 20 ml of absolute methanol, and a 20% solution of sodium methylate in methanol was added. The methanol was driven off in vacuo to dryness. The remaining thick residue was dissolved in 25 ml of anhydrous toluene, and the latter was driven off until the distillate was completely transparent. Heating on a boiling water bath was continued for 4 hours. The toluene was driven off, and the residue heated for another 4 hours with 25 ml of absolute toluene.

After the toluene had been driven off in vacuo, the residue was dissolved in 100 ml of water, treated with charcoal, filtered, chilled, and then acidulated with hydrochloric acid until its reaction with Congo red was weakly acid. The next day the resultant crystals were filtered out, dried, and washed with ether. M.p. 168-169° (with decomposition). The mixed melting point with the initial compound exhibited no depression.

2-(α-Phenyl-α-carbomethoxymethyl)-thiazolidine-4-carboxylic acid. The methyl ester of formylphenylacetic acid, prepared by the method described in the literature [7], was used in a mixture of the α and β forms.

5.5 grams of l-cysteine hydrochloride, 5.7 g of methyl formylphenylacetate, and 2 ml of water were heated and vigorously stirred on a boiling water bath for 15 minutes. The reaction mass was gradually poured into 100 ml of cold water, and 25 ml of an 8% solution of sodium bicarbonate was slowly added. The next day the crystalline precipitate was filtered out, washed with water, and dried, the dry substance being washed with ether. M.p. 170-171° (with decomposition).

6.144 mg substance: 0.280 ml N_2 (21.8°, 729.6 mm). 6.737 mg substance: 0.297 ml N_2 (22.3°, 728.5 mm). Found %: N 5.07, 4.89. $C_{13}H_{15}O_4NS$. Calculated %: N 4.98.

When the free acid was heated to 160-170°, it was decarboxylated as in the case of the carbethoxy analog.

Saponifying ethyl formylphenylacetate. 2 grams of the ester was dissolved in 25 ml of alcohol, 24 ml of a 1N solution of sodium hydroxide was added, and the whole was allowed to stand at room temperature for 48 hours. Then 24 ml of a 1N solution of hydrochloric acid was added, and the solution was evaporated in vacuo on a water bath. Lustrous lamellar crystals with an m.p. of 76° soon settled out. Their mixed melting point with phenylacetic acid exhibited no depression.

Diethyl acetal of ethyl formylphenylacetate. 80 grams of ethyl formylphenylacetate was dissolved in 300 ml of absolute ethyl alcohol, and 3 g of hydrogen chloride was passed through the solution, after which the solution was refluxed for 3 hours. When it had cooled, 10 g of a 50% solution of potassium hydroxide was added, the precipitated potassium chloride being filtered out 10 minutes later, the alcohol driven off in vacuo, and the residual oil dissolved in 200 ml of ether. The ether solution was washed at 0° with 120 ml of a 10% solution of potassium hydroxide and then with water, and dried with sodium sulfate, after which the ether was driven off. The residue was fractionated, a fraction with a b.p. of 142-143° at 9-10 mm being collected. The yield totaled 40 g. A colorless oil with an extremely faint odor and a sp.gr. of 1.0397 at 20°.

5.149 mg subs.: 12.875 mg CO_2; 3.578 mg H_2O. 4.600 mg subs.: 11.504 mg CO_2; 3.233 mg H_2O. Found %: C 68.19, 68.2; H 7.76, 7.86. $C_{15}H_{22}O_4$. Calculated %: C 67.67; H 8.36.

Diethyl acetal of formylphenylacetic acid. 40 g of the diethyl acetal of ethyl formylphenylacetate, 120 ml of methanol, 20 g of a 50% solution of sodium hydroxide, and 10 ml of water were allowed to stand for two days at 15-20°. Then the methanol was driven off in vacuo on a water bath. The remaining solution was diluted with 200 ml of water and extracted 3 times with ether, the extracts being discarded.

The ether was driven out of the aqueous solution of the product, which was treated with 2 g of activated charcoal and filtered, the filtrate being carefully neutralized at 0° with hydrochloric acid until its reaction with Congo red was weakly acid. The resulting crystalline precipitate was filtered out, washed thoroughly with cold water, dried in a vacuum desiccator, and recrystallized from toluene. The yield totaled 25 g, with a m.p. of 121-123° (with decomposition). Lamellae, freely soluble in alcohol and ether, less so in benzene.

0.1033 g subs.: 4.6 ml 0.1 N NaOH. 0.0544 g subs.: 2.35 ml 0.1 N NaOH. Found %: COOH 20.04, 19.44; OC_2H_5 38.38. $C_{13}H_{18}O_4$. Calculated %: COOH 18.91; OC_2H_5 38.38.

When the diethyl acetal of formylphenylacetic acid was heated in vacuo on an oil bath at 140-150°, a substance with a b.p. of 85-88° at 11 mm was driven off. A colorless oil with a geranium odor that exhibited a silver mirror reaction. It was identified as phenylacetaldehyde [8].

4.317 mg subs.: 12.689 mg CO_2; 2.765 mg H_2O. Found %: C 80.16; H 7.18. C_8H_8O. Calculated %: C 80.00; H 6.71.

Oxymethylenephenylacetic acid. 9 g of the diethyl acetal of formylphenylacetic acid was mixed with 25 ml of conc.hydrochloric acid at 0° in a 50-ml round-bottomed flask for 5 hours while anhydrous hydrogen chloride was passed through the flask. The reaction mass thickened. 50 ml of cold water was added, and the precipitate was filtered out 30 minutes later and thoroughly washed with ice water. Then it was dried in a vacuum desiccator. Prisms with a m.p. of 101-103°, which had the odor of phenylacetaldehyde (geranium). The substance was washed with light petroleum ether. It was freely soluble in all the ordinary organic solvents, with the exception of gasoline.

The pungent odor of phenylacetyldehyde appeared when it was heated with water or when it was stored. It had the oxymethylene form, an aqueous solution being turned a strong blue by ferric chloride. Ammoniacal silver nitrate was hardly reduced at all by it. It decolorized a bromine solution. It was rapidly decarboxylated in pyridine, yielding phenylacetaldehyde.

4.504 mg subs.: 11.019 mg CO_2; 1.846 mg H_2O. 4.173 mg subs.: 10.210 mg CO_2; 1.772 mg H_2O. Found %: C 66.72, 66.73; H 4.59, 4.75. C_9H_8O. Calculated %: C 65.85; H 4.87.

2-Benzylthiazolidine-4-carboxylic acid. 0.9 g of l-cysteine hydrochloride, 1 g of oxymethylenephenylacetic acid, and 4 ml of methanol were mixed together, and the resulting solution was allowed to stand at room temperature. Carbon dioxide began to be given off within a few minutes. Two days later the mass was gradually poured into 20 ml of water, carefully neutralized with 5 ml of an 8% solution of sodium bicarbonate until its reaction with Congo red was weakly acid, and then diluted 1:1 with acetone. The resultant crystalline precipitate was filtered out, washed with water and dried in a vacuum desiccator. A small amount of the substance was quickly recrystallized from hot water. Thin, elongated needles with a m.p. of 154-165° (with decomposition). Sparingly soluble in water, more so in ether and alcohol, insoluble in gasoline.

5.950 mg subs.: 0.285 ml N_2 (19°, 738 mm). 0.5743 g subs.: 0.0758 g H_2O. Found %: N 5.43; H_2O 13.2. $C_{11}H_{13}O_2NS \cdot 2H_2O$. Calculated %: N 5.4; H_2O 13.89.

The same substance was secured by condensing 1 g of cysteine hydrochloride at 50° for 8 hours with 0.9 g of phenylacetaldehyde in 1 ml of water and 5 ml of methanol, as well as by condensing the cysteine hydrochloride with oxymethylenephenylacetic acid in pyridine.

2-(α-Phenyl-α-carboxymethyl)-thiazolidine-4-carboxylic acid.* 2 g of l-cysteine hydrochloride was heated with 0.8 ml of water and 3 g of the diethyl acetal of formylphenylacetic acid were heated and stirred together for 5 minutes on a boiling water bath. At first the mass foamed a little, but then boiled up, giving off alcohol vapor and became homogeneous. It crystallized quickly upon cooling. The crystalline mass was treated with 50 ml of acetone, the crystals being filtered out and washed with acetone. The substance was recrystallized from 90% of acetone. Short little needles with a m.p. of 169-170° (with decomposition). Freely soluble in hot water, soluble in methanol, and insoluble in acetone, benzene, and chloroform. When boiled in water it decomposed into cysteine, phenylacetaldehyde, and carbon dioxide.

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* This synthesis could not be repeated.

10.072 mg subs: 3.86 mg 0.01 N H_2SO_4. 0.0804 g subs.: 6.0 ml 0.1 N NaOH. 0.0688 g subs.: 5.15 ml 0.1 N NaOH. Found %: N 5.37; COOH 33.57, 33.68. $C_{12}H_{13}O_4NS$. Calculated %: N 5.24; COOH 33.69.

S-β-(α-Phenyl-α-carboxy)-ethylenecysteine. 3 g of the diethyl acetal of formylphenylacetic acid was stirred at 0° for 3 hours with 20 ml of concentrated hydrochloric acid. 2 g of dl-cysteine hydrochloride was added to the reaction mass, and stirring was continued for 3 more hours at from 0° to 5°, the oxymethylenephenylacetic acid dissolving. The reaction with sodium nitroprusside for a free mercapto group was negative. The solution was then evaporated in vacuo to dryness. A crystalline deposit was left on the wall of the flask, which was dissolved in 15 ml of water; the solution was neutralized until its reaction with Congo red was barely acid, a very thick oil that gradually crystallized settling out. The substance was recrystallized from hot water. Needles with a m.p. of 164-165° (with decomposition).

This same compound was precipitated by adding sodium carbonate to a solution of its hydrochloride. It was freely soluble in hydrochloric acid, sparingly soluble in water and methanol, and insoluble in chloroform, acetone, toluene, ethyl acetate, and gasoline.

7.304 mg subs.: 0.304 ml N_2 (23.5°, 747 mm). 11.309 mg subs.: 4.04 ml 0.01 N H_2SO_4. 11.434 mg subs.: 3.93 ml 0.01 N H_2SO_4. 0.1266 g subs.: 0.1108 g $BaSO_4$. Found %: N 4.87, 5.00, 4.81; S 12.01. $C_{12}H_{13}O_4NS$. Calculated %: N 5.24; S 11.98.

0.4 g of the substance was dissolved in 20 ml of water containing 4 ml of an 8% solution of sodium bicarbonate. The solution was heated to 70° for 1.5 hours, after which it was treated with charcoal, filtered, and acidulated at 0° with 10% H_2SO_4 until its reaction with Congo red was weakly acid. A crystalline precipitate (clusters) gradually settled out. The next day the substance was filtered out and purified by converting it into a sodium salt. Its mixed melting point with S-β-(α-phenyl-α-carboxy)-ethylenecysteine exhibited no depression.

Ethylmethoxymethylenephenylacetate. 13 g of ethyl oxymethylenephenylacetate was added to 60 ml of a 5% solution of sodium hydroxide chilled to 0°; the whole was agitated vigorously and then the undissolved substance was extracted 2 or 3 times with ether, which was discarded. 7 g of dimethyl sulfate was added to the aqueous solution, and the reaction mass was thoroughly stirred for 12 hours at 15-20°. The supernatant oil was extracted with ether. The ether extract was washed with a solution of sodium bicarbonate and dried with sodium sulfate, the ether was driven off, and the remaining oil was distilled in vacuo, a fraction with a b.p. of 124-125° at 3 mm being collected. The yield was 6.8 g.

S-β-(α-Phenyl-α-carbethoxy)-ethylene-dl-cysteine hydrochloride. 6.5 g of ethyl methoxymethylenephenylacetate was stirred at 0° with 5 g of dl-cysteine hydrochloride and 10 ml of conc. hydrochloric acid, and hydrogen chloride was passed through the reaction mass for 1 hour, after which stirring was continued for another 2 hours. A white crystalline substance settled out after some time had passed. The mass was diluted with an equal quantity of water, and the crystals were filtered out, washed thoroughly with 20% hydrochloric acid, and dried in a vacuum desiccator over alkali and sulfuric acid. The substance was dissolved in acetone, and the solution was treated with ether, a white crystalline precipitate weighing 6.2 g with a m.p. of 169-172° (with decomposition) settling out.

The substance was freely soluble in water and methanol, somewhat less in acetone, and only very slightly soluble in ether and toluene. The substance was precipitated from aqueous solutions when conc. hydrochloric acid was added. Its nitroprusside reaction for a mercapto group was negative, and it could not be titrated with iodine.

7.359 mg subs.: 2.16 ml 0.01 N H_2SO_4. 9.631 mg subs.: 2.86 ml 0.01 N H_2SO_4. Found %: N 4.11, 4.16; S 9.7; Cl 10.65, 10.81. $C_{14}H_{18}O_4NSCl$. Calculated %: N 4.22; S 9.65; Cl 10.71.

S-β-(α-Phenyl-α-carbethoxy)-ethylene-dl-cysteine. 2 g of S-β-(α-phenyl-α-carbethoxy)-ethylene-dl-cysteine hydrochloride was dissolved in 10 ml of methanol, and 0.7 ml of pyridine was added. The next day the precipitated crystals were filtered out and washed with methanol and ether. Thin lamellae with a m.p. of 153-154° (with decomposition). The substance was sparingly soluble in cold water and more soluble in hot, sparingly soluble in methanol and ethyl alcohol, and insoluble in acetone, benzene, and gasoline; it was soluble in dilute alkalies and mineral acids. Its ninhydrin reaction for an α-amino acid was positive. It contained no mercapto group, nor was it titrated by iodine. When it was dissolved in a 5% sodium hydroxide solution, a nitroprusside reaction indicated the presence of a mercapto group. It formed no precipitate when reacted with mercurous chloride in an alcoholic solution.

11.466 mg subs.: 3.88 ml 0.01 N H_2SO_4. Found %: N 4.74. $C_{14}H_{17}O_4NS$. Calculated %: N 4.74.

0.6 g of the substance was dissolved by heating it in 10 ml of a 2% solution of sodium bicarbonate. The solution was heated to 70° on a water bath for 1.5 hours. Then the solution was chilled to 0° and acidulated with 2% hydrochloric acid. The resultant flocculent precipitate was filtered out, washed with water, dried, and recrystallized from methanol. Needles with a m.p. of 169-170° (with decomposition). Their mixed melting point with 2-(α-phenyl-α-carbethoxymethyl)-thiazolidine-4-carboxylic acid exhibited no depression.

The thiazolidine compound was also produced by treating S-β-(α-phenyl-α-carbethoxy)-ethylene-dl-cysteine with aqueous ammonia.

S-β-(α-Phenyl-α-carbethoxy)-ethylene-N-acetylcysteine. 1 g of S-β-(α-phenyl-α-carbethoxy)-ethylenecysteine was gradually added to 3 ml of anhydrous pyridine that contained 0.5 g of acetic anhydride. The substance dissolved after it had been stirred for 1 hour. Then the solution was gradually added to 12 ml of 20% sulfuric acid at 0°. The thick yellow oil that separated out was extracted with ether. The ether extract was washed with 10 ml of water and then agitated violently for 5 minutes with 10 ml of a 4% sodium bicarbonate solution. The aqueous solution was separated chilled to 0°, and acidulated with 3 ml of 10% sulfuric acid, the white emulsion that resulted being extracted with ether. The ether solution was washed with water and dried over sodium sulfate, and the ether was driven off in vacuo. This left a pale-yellow mass with a m.p. of 48-52°. It was very freely soluble in methanol butyl alcohol, ether, ethyl acetate, acetone, and chloroform, sparingly soluble in toluene, and insoluble in petroleum ether and dilute sulfuric acid.

8.582 mg subs.: 2.6 ml 0.01 N H_2SO_4. 0.0505 g subs.: 1.5 ml 0.1 N NaOH (in methyl alcohol).
Found %: N 4.24; COOH 13.36. $C_{16}H_{19}O_5NS$. Calculated %: N 4.15; COOH 13.3.

S-β-(α-Phenyl-α-carbomethoxy)-ethylenecysteine hydrochloride. We used methyl formylphenylacetate instead of methyl methoxymethylenephenylacetate in synthesizing the above compound. The yield was lower, since only the oxymethylene form reacts with cysteine hydrochloride, yielding an S-substitution derivative of cysteine. 2.5 g of cysteine hydrochloride was stirred with 2.8 g of methyl formylphenylacetate and 10 ml of conc. hydrochloric acid for 6 hours at 0°. A precipitate began to settle out toward the end of the reaction. The next day the precipitate was filtered out, washed three times with hydrochloric acid, dried in a vacuum desiccator, dissolved in acetone, and precipitated with ether. The substance was recrystallized from hydrochloric acid, dried, and washed with acetone and ether. M.p. 169-172° (with decomposition). Its physical and chemical properties were the same as those of its carbethoxy analog mentioned above. The yield was 1.2 g.

0.1869 g subs.: 0.1318 g $BaSO_4$. Found %: S 9.68. $C_{13}H_{16}O_4NSCl$. Calculated %: S 10.07.

S-β-(α-Phenyl-α-carbomethoxy)-ethylenecysteine. 4.2 g of the hydrochloride was dissolved in 21 ml of methanol, and 2.1 g of pyridine was added. The next day the crystalline precipitate was filtered out and washed with methanol and ether. The yield totaled 2.55 g with a m.p. of 151-153° (with decomposition). Its properties resembled those of S-β-(α-phenyl-α-carbethoxy)-ethylenecysteine.

7.393 mg subs.: 0.332 ml N_2 (20.5°, 743 mm). Found %: N 5.11. $C_{13}H_{15}O_4NS$. Calculated %: N 4.98.

0.3 g of S-β-(α-phenyl-α-carbomethoxy)-ethylene cysteine was mixed with 3 ml of anhydrous pyridine and 0.15 g of triethylamine and set aisde to stand for 3 days, the precipitate gradually dissolving. The solution was poured into 12 ml of a 25% solution of sulfuric acid, the resulting white precipitate being dissolved in 20 ml of ether. The ether solution was discarded. A substance with a m.p. of 172-173° (with decomposition) crystallized gradually from the aqueous solution. Its mixed melting point with 2-(α-phenyl-α-carbomethoxymethyl)-thiazolidine-4-carboxylic acid exhibited no depression.

2-(α-Phenyl-α-carbomethoxymethyl)-N-acetylthiazolidine-4-carboxylic acid. 2 g of 2-(α-phenyl-α-carbomethoxymethyl)-thiazolidine-4-carboxylic acid was mixed with 5 g of absolute anhydrous pyridine, and 1.5 ml of acetic anhydride was added. The next day the reaction mass was gradually added to 40 ml of 10% sulfuric acid chilled to 0°. The white precipitate was filtered out, washed with water dissolved in a dilute aqueous solution of ammonia, and treated with charcoal, the resultant solution being poured into 30 ml of 10% sulfuric acid at 0°. The precipitate was filtered out, washed with water, dried, and recrystallized from a small quantity of methanol. Thin, elongated needles with a m.p. of 222-223° (with decomposition).

6.505 mg subs.: 0.249 ml N_2 (16°, 724 mm). Found %: N 4.34. $C_{15}H_{17}O_5NS$. Calculated %: N 4.34.

2-(α-Phenyl-α-carboxymethyl)-N-acetylthiazolidine-4-carboxylic acid. 1.5 g of the substance was dissolved in 10 ml of a 10% solution of sodium hydroxide and set aside for 2 days at room temperature. The solution was chilled to 0° and acidulated with 10% sulfuric acid. The oil that separated was extracted with 250 ml of ether. The ether solution was washed with a small quantity of water and dried with anhydrous sodium sulfate, after which the ether was driven off to a total volume of 10 ml. The resultant white crystalline precipitate weighed 0.6 g. Needles with a m.p. of 206-207° (with swelling). Freely soluble in water and methanol, less so in ether.

5.024 mg 0.207 ml N_2 (18°, 748.5 mm). Found%: N 4.76. $C_{14}H_{15}O_5NS$. Calculated %: N 4.53.

SUMMARY

1. Condensing *dl*-cysteine with ethyl formylphenylacetate yielded 2-(α-phenyl-α-carbethoxymethyl)-thiazolidine-4-carboxylic acid, from which no compound containing a thiazolidine-β-lactam ring system could be obtained.

2. Oxymethylenephenylacetic acid has been obtained from the diethyl acetal of ethyl formulphenylacetate. Condensing this acid with *l*-cysteine yielded 2-benzylthiazolidine-4-carboxylic acid.

3. When *dl*-cysteine was reacted with oxymethylenephenylacetic acid in concentrated hydrochloric acid, S-β-(α-phenyl-α-carboxy)-ethylenecysteine was produced.

4. Reacting *dl*-cysteine with ethyl methoxymethylenephenylacetate in concentrated hydrochloric acid yielded S-β(α-phenyl-α-carbethoxy)-ethylenecysteine, which could be readily converted into 2-(α-phenyl-α-carbethoxymethyl)-thiazolidine-4-carboxylic acid.

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Received September 20, 1950

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THE NITRATION OF ac-1-TETRAHYDRONAPHTHOIC ACID AND THE TRANSFORMATIONS OF NITRO-ac-1-TETRAHYDRONAPHTHOIC ACIDS

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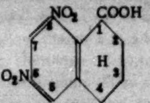
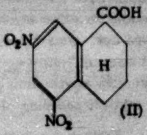
Our researches on the carboxylic and thiocarboxylic acids of tetrahydronaphthalene [1] up to now have dealt principally with compounds having substituents in the aromatic part of the ring: we thought it would be interesting to make a study of acids that had functional groups in both parts of the tetrahydronaphthalene molecule (both the hydrogenated and the nonhydrogenated). The initial substance used for synthesizing these compounds in the present research was ac-1-tetrahydronaphthoic acid, which was nitrated. The nitration of this acid, which had been not been previously investigated, interested us not only as a means of securing compounds of the specified type, but also as providing the opportunity of pursuing our study of the group orientation phenomena in the tetralin ring.

Nitration of ac-1-tetrahydronaphthoic acid with nitric acid (sp.gr. 1.5) produced a dinitro acid, the yield being 90%, while when the sp.gr. of the nitric acid used was 1.4, we secured a mixture of mononitro acids, with a yield of 70%. The method we have developed was employed to separate this mixture into two mononitro acids, one with a m.p. of 143° and the other with a m.p. of 163°. Renitration of each of these mononitro acids produced the same dinitro acid, identical with the dinitro acid secured when the ac-1-tetrahydronaphthoic acid was directly nitrated with fuming nitric acid.

We determined the positions at which the nitro groups entered by employing the transformations of the nitro acids that either led directly to substances of known structure or established a genetic relationship between the latter and the initial nitro compounds. One of these transformations is the following: oxidizing the dinitro tetrahydronaphthoic acid, which yielded 3,5-dinitrophthalic acid, evidence of the meta position of the nitro groups to each other in the initial dinitro-1-tetrahydronaphthoic acid; hence, one of the formulas given below (I and II) may be assigned to the latter:



(I)



(II)

The nitro groups in the mononitro acids were reduced catalytically, the nitro acid with a m.p. of 143° yielding amino-1-tetrahydronaphthoic acid with a m.p. of 200.5-201.5°, and the nitro acid with a m.p. of 163° yielding an amino acid with a m.p. of 170-171°.

Of the amino-ac-1-tetrahydronaphthoic acids, only one has been described in the literature so far—8-amino-ac-1-tetrahydronaphthoic acid [2]. The physicochemical properties of this amino acid and of its derivatives were not the same as the constants of the amino acids we had synthesized or their derivatives; therefore, the nitro and amino groups could not occupy the 8 position in our compounds, which determined the composition of the dinitro acid first of all: it could be nothing but 5,7-dinitro-(1,2,3,4)-tetrahydro-1-naphthoic acid. Since this same dinitro acid was produced by renitrating each of the two isomeric mononitro acids, one of the latter had to be 5-nitro-(1,2,3,4)-tetrahydro-1-naphthoic acid, and the other 7-nitro-(1,2,3,4)-1-tetrahydronaphthoic acid, though we did not know which was which. To ascertain the structure of the mononitro acids we synthesized the 5-amino-1-naphthoic acid described in the literature [3] and reduced it with sodium and isoamyl alcohol. Since in this method of reduction the amino and carboxyl groups at the α-positions in naphthalene orient the hydrogen to the part of the ring where the carboxyl group is located, we might expect 5-amino-(1,2,3,4)-tetrahydro-1-naphthoic acid, identical with one of our amino acids, to be formed. As a matter of fact, the reaction resulted in formation of an amino acid with a m.p. of 200-201°, which was identical with the amino acid we had synthesized by reducing the mononitro acid with a m.p. of 143°; it followed that the latter and its respective amino acid were 5-nitro-(amino)-1,2,3,4-tetrahydro-1-naphthoic acids.

The sum total of all these findings also indicated that the second mononitro acid, with a m.p. of 163°, and its corresponding amino acid were nothing else than 7-nitro-(amino)-tetrahydro-1-naphthoic acids. The β-position of the amino group in the 7-amino-1-tetrahydronaphthoic acid was likewise confirmed by the fact that its decarboxylation yielded the well-known ar-β-tetrahydronaphthylamine.

In addition to the conversions required to determine the structure of the compounds we had synthesized, we also carried out a few others: the 5,7-dinitro-1-tetrahydronaphthoic acid was reduced to 5,7-diamino-1-tetrahydronaphthoic acid, decarboxylation of which yielding the corresponding diamine; and we synthesized the 5(7)-nitro-1-tetrahydrothionaphthoic acids and the simplest derivatives of all the nitro and amino acids referred to above.

EXPERIMENTAL

5-Nitro-ac-tetrahydro-1-naphthoic acid and 7-nitro-ac-tetrahydro-1-naphthoic acid. 60 g of ac-tetrahydro-1-naphthoic acid was added in one batch to 350 ml of HNO_3 (sp.gr. 1.40). The mixture was heated gently to set off the reaction. The temperature within the reaction mixture was maintained at 40-41°. The ac-tetrahydro-1-naphthoic acid dissolved gradually, a crystalline precipitate of the nitro compounds beginning to settle out after some time. 1.5 hours later the reaction mixture was cooled to room temperature.

The precipitate was suction-filtered and washed, first with nitric acid, sp.gr. 1.40, and then with water. This yielded 39 g of a slightly yellowish crystalline substance with a m.p. of 115-122°. The acid mother liquor was highly diluted with water. A tarry mass settled out, which solidified after some time had elapsed. The resultant yellow substance was filtered out and recrystallized from toluene. This yielded 10 g of a substance with a m.p. of 115-122°. Neutralization of the diluted nitric acid solution with soda yielded another 3 g of a substance with a lower melting point. When 60 g of ac-tetrahydro-1-naphthoic acid was nitrated, for example, we secured 52 g of a mixture of isomeric nitro acids. The yield was 69% of the theoretical.

The mixture of nitro acids produced by nitration dissolved readily in a 10% soda solution. When the alkaline solutions were fractionally acidulated with dilute hydrochloric acid, the first nitro acid to settle out was the one with the higher melting point – 7-nitro-(1,2,3,4)-1-tetrahydronaphthoic acid. Its m.p. was 163° after recrystallization from toluene. As acidulation was continued, 5-nitro-(1,2,3,4)-1-tetrahydronaphthoic acid settled out, its melting point being 143° after recrystallization from toluene[*], while the last precipitate was a mixture of the same isomers, with a m.p. of 110-130°, which could not be separated by this method.

Separating isomeric nitrotetrahydronaphthoic acids via their ethyl esters. 52 g of a mixture of isomeric 5- and 7-nitro-ac-tetrahydro-1-naphthoic acids, with a m.p. of 115-122°, was heated for 8 hours with 500 ml of absolute ethyl alcohol and 15 ml of concentrated sulfuric acid. When the reaction was over the bulk of the alcohol was driven off, a small quantity of water was added to the residue, and the resultant oil was extracted with ether. The ether solution was washed with a soda solution and then with water. The aqueous alkaline solution was acidified. This yielded 1 g of a mixture of nitro acids that had not entered into the esterification reaction. The ether solution was dried over anhydrous Na_2SO_4, after which the ether was driven off as completely as possible. A small quantity of petroleum ether was added to the residue and the mixture was chilled with ice. The resulting precipitate was filtered out. This yielded 16 g of a slightly yellowish crystalline substance with a m.p. of 77-78°, constituting the ethyl ester of 7-nitro-ac-tetrahydro-1-naphthoic acid. The ethyl ester with a m.p. of 77-78° was saponified by heating it with 40% acetic acid and a small amount of hydrochloric acid. Upon cooling, 7-nitro-ac-tetrahydro-1-naphthoic acid crystallized out; its m.p. was 163° after recrystallization from toluene.

7-Nitro-ac- tetrahydro-1-naphthoic acid consisted of nearly colorless crystals, which were freely soluble in alcohol and hot toluene, and slightly soluble in cold toluene and carbon tetrachloride.

6.629 mg subs.: 0.366 ml N_2 (20.5°, 733.0 mm). 6.648 mg subs.: 0.372 ml N_2 (23.0°, 740.0 mm). 3.877 mg subs.: 8.522 mg CO_2; 1.771 mg H_2O. Found %: C 59.94; H 5.11; N 6.19, 6.28. $C_{11}H_{11}O_4N$. Calculated %: C 59.74; H 4.97; N 6.34.

The petroleum ether mother liquor, which contained the ethyl ester of 5-nitro-ac-tetrahydro-1-naphthoic acid with a trace of the ethyl ester of the 7-nitro acid, was evaporated until the solvent had been driven off. The liquid residue was saponified by heating it with dilute acetic acid (40%) containing a small percentage of hydrochloric acid. The customary treatment yielded a mixture of nitro acids with a m.p. of 120-133°. The mixture of nitro acids was dissolved in a 10% soda solution, and dilute hydrochloric acid was gradually added to the resultant solution. At first 5-nitro-ac-tetrahydro-1-naphthoic acid settled out, its m.p. being 143° after recrystallization from toluene. The amount of the 5-nitro acid secured was about half the mixture initially used. As acidification continued, a mixture of nitro acids with a m.p. of 123-133° settled out. This mixture was re-esterified, the entire process of precipitating and separating the isomeric esters and acids described above being repeated.

Double esterification and saponification of 52 g of the mixture yielded 14 g of 7-nitro-ac-tetrahydro-1-naphthoic acid and 17 g of 5-nitro-ac-tetrahydro-1-naphthoic acid. 5-Nitro-ac-tetrahydro-1-naphthoic acid consisted of crystals with a greenish tinge, m.p.143°, freely soluble in acetone, ether, alcohol, and hot toluene, and sparingly soluble in cold toluene.

8.380 mg subs.: 0.477 ml N_2 (25.5°, 732.0 mm). 3.071 mg subs.: 6.747 mg CO_2; 1.369 mg H_2O. Found %: C 59.92; H 4.99; N 6.27. $C_{11}H_{11}O_4N$. Calculated %: C 59.74; H 4.97; N 6.34.

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[*] Separating the nitro acids by this method led us to assume that their acidities differed; further research (see the following experiment) and potentiometric titration, however, indicated that their acidities were identical. The sequence in which the isomers were precipitated from aqueous alkaline solutions depended, apparently, upon quantitative relationships.

Ethyl ester of 5-nitro-ac-tetrahydro-1-naphthoic acid. 4.5 g of 5-nitro-ac-tetrahydro-1-naphthoic acid was heated to boiling for 8 hours with 40 ml of absolute ethyl alcohol and 3 drops of conc. sulfuric acid. When the reaction was over, the alcohol was driven off, and the residue extracted with ether. The ether solution was washed with a soda solution and with water and then dried with anhydrous sodium sulfate. The ether was driven off, and the residue (4 g) distilled in vacuo.

The ethyl ester of 5-nitro-ac-tetrahydro-1-naphthoic acid, was a greenish oil, with a b.p. of 171° at 1.5-2 mm; d_4^{20} 1.2140, n_D^{20} 1.5428.

5.223 mg subs.: 0.275 ml N_2 (30.0°, 724.0 mm). Found %: N 5.64. $C_{13}H_{15}O_4N$. Calculated %: N 5.62.

5-Nitro-ac-tetrahydro-1-naphthoyl chloride. 3.0 g of 5-nitro-ac-tetrahydro-1-naphthoic acid, with a m.p. of 143°, was heated to boiling with 9 ml of thionyl chloride for 3 hours. When the reaction was over, the excess thionyl chloride was driven off. The last traces of the thionyl chloride were eliminated by adding some absolute benzene, which was then likewise driven off in vacuo. A small quantity of petroleum ether was added to the residual mass, and the mixture was strongly chilled with ice and salt. Vigorous rubbing with a glass rod threw down a crystalline precipitate, which was filtered out and recrystallized from ligroin.

5-Nitro-ac-tetrahydro-1-naphthoyl chloride consisted of colorless needles with a m.p. of 53-54°, which were readily soluble in benzene and acetone, though only slightly soluble in ligroin and petroleum ether.

0.1457 g subs.: 0.0864 g AgCl. Found %: Cl 14.67. $C_{11}H_{10}O_3NCl$. Calculated %: Cl 14.82.

Diethylaminoethyl ester of 5-nitro-ac-tetrahydro-1-naphthoic acid (hydrochloride). 1.17 g of diethylaminoethanol was added to a solution of 3 g of 5-nitro-ac-tetrahydro-1-naphthoyl chloride in 50 ml of absolute benzene, and the mixture was heated to boiling for 3 hours. The hydrochloride that settled out upon cooling was dissolved in 2-3 ml of absolute ethyl alcohol, and absolute ether was added to the alcoholic solution until precipitation was complete. This yielded 3.4 g with a m.p. of 120-122°. Reprecipitation from alcohol by ether yielded the hydrochloride of the diethylaminoethyl ester of 5-nitro-ac-tetrahydro-1-naphthoic acid as a colorless, nonhygroscopic substance with a m.p. of 125-127°, which was readily soluble in water and alcohol, and sparingly so in benzene and chloroform.

8.115 mg subs.: 0.547 ml N_2 (21.5°, 740.0 mm). 7.140 mg subs.: 0.490 ml N_2 (21.5°, 738.0 mm). Found %: 7.62, 7.73. $C_{17}H_{24}O_4N_2 \cdot HCl$. Calculated %: N 7.85.

Ethyl ester of 7-nitro-ac-tetrahydro-1-naphthoic acid. 1 g of 7-nitro-ac-tetrahydro-1-naphthoic acid was heated to boiling for 8 hours with 10 ml of absolute ethyl alcohol and 3 drops of conc. sulfuric acid. The usual processing yielded the ethyl ester of 7-nitro-ac-tetrahydro-1-naphthoic acid as colorless, silky, elongated needles with a m.p. of 77-78°. Readily soluble in ether, alcohol, and chloroform, soluble when heated in petroleum ether, and rather slightly soluble in petroleum ether in the cold.

8.211 mg subs.: 0.418 ml N_2 (29.5°, 730.5 mm). Found %: N 5.52. $C_{13}H_{15}O_4N$. Calculated %: N 5.62.

7-Nitro-ac-tetrahydro-1-naphthoyl chloride. 3.0 g of 7-nitro-ac-tetrahydro-1-naphthoic acid was heated to boiling for 3 hours with 9 ml of thionyl chloride. The subsequent processing was like that described for the 5-nitro isomer.

When recrystallized from ligroin, the 7-nitro-ac-tetrahydro-1-naphthoyl chloride consisted of colorless needles with a m.p. of 97-98°, which were freely soluble in benzene and, when heated, in ligroin, and sparingly soluble in cold ligroin and in petroleum ether.

0.1287 g subs.: 0.0759 g AgCl. 0.1582 g subs.: 0.0937 g AgCl. Found %: Cl 14.57, 14.65. $C_{11}H_{10}O_3NCl$. Calculated %: Cl 14.82.

Diethylaminoethyl ester of 7-nitro-ac-tetrahydro-1-naphthoic acid (hydrochloride). The reaction conditions were the same as those employed in the synthesis of the alkamino ester of 5-nitro-ac-tetrahydro-1-naphthoic acid.

3.0 g of 7-nitro-ac-tetrahydro-1-naphthoyl chloride and 1.17 g of diethylaminoethanol yielded 3.4 g of the hydrochloride of the diethylaminoethyl ester of 7-nitro-ac-tetrahydro-1-naphthoic acid: a colorless, crystalline substance with a m.p. of 134-136°. freely soluble in water and alcohol, sparingly soluble in benzene and chloroform, and insoluble in ether.

7.730 mg subs.: 0.549 ml N_2 (21.5°, 740.0 mm). 6.270 mg subs.: 0.447 ml N_2 (22.5°, 738.0 mm). Found %: N 8.01, 7.89. $C_{17}H_{24}O_4N_2 \cdot HCl$. Calculated %: N 7.85.

5-Amino-ac-tetrahydro-1-naphthoic acid and its derivatives. a) 2.21 grams of 5-nitro-ac-tetrahydro-1-naphthoic acid was dissolved in 100 ml of methanol, 5 g of Raney's nickel catalyst was added to the solution, and the mixture was agitated in a hydrogen atmosphere until the requisite amount of hydrogen (670 ml) had been absorbed. Reduction was carried out either at room temperature or with gentle heating to 25°. After the hydrogen had been absorbed, the catalyst was filtered out, and the alcohol was driven off in vacuo. The amino acid was recrystallized from alcohol. This yielded 1.55 g of a substance with a m.p. of 200.5-201.5° (with decomposition).

5-Amino-ac-tetrahydro-1-naphthoic acid was a colorless substance that was slightly soluble in methanol and ethyl alcohol, even less soluble in acetone and chloroform, and wholly insoluble in ether.

8.437 mg substance: 0.546 ml N_2 (25.0°, 742.0 mm). Found %: N 7.24. $C_{11}H_{13}O_2N$. Calculated %: N 7.33.

5-Acetamino-ac-tetrahydro-1-naphthoic acid was synthesized by heating 5-amino-ac-tetrahydro-1-naphthoic acid with acetic anhydride in ethyl acetate for 3 hours. After the reaction was over, the precipitated acetyl derivative was filtered out and recrystallized from aqueous alcohol.

5-Acetamino-ac-tetrahydro-1-naphthoic acid was a colorless crystalline substance with an m.p. of 232-232.5° (with decomposition), which was insoluble in ethyl acetate, and soluble in methanol and ethyl alcohol.

7.947 mg substance: 0.422 ml N_2 (22.0°, 736.0 mm). Found %: N 5.95. $C_{13}H_{15}O_3N$. Calculated %: N 6.01.

b) The 5-Amino-1-naphthoic acid [1] was dissolved in 250 ml of hot absolute isoamyl alcohol, and 15 ml of metallic sodium was added to the hot solution (boiling of the isoamyl alcohol being continued throughout the reaction). After all the sodium had dissolved, the isoamyl alcohol was driven off with steam.

The remaining aqueous-alkaline solution was neutralized with acid (using litmus paper) and then filtered. The filtrate was evaporated in vacuum and cooled, a crystalline mass of sodium acetate being thrown down. The minimum quantity of water was added to dissolve the latter. The insoluble brown precipitate was filtered out. This yielded 2.3 g of a substance with an m.p. of 180-190°.

Double recrystallization from alcohol raised the m.p. of the substance to 200-201° (with decomposition): it proved to be 5-amino-ac-tetrahydro-1-naphthoic acid. Its mixed melting point with the 5-amino-ac-tetrahydro-1-naphthoic acid we had synthesized by another method was 200.5-201.5° (with decomposition).

8.793 mg substance: 0.574 ml N_2 (24.0°, 743.0 mm). 8.578 mg substance: 0.549 ml N_2 (24.0°, 743.0 mm). Found %: N 7.33, 7.19. $C_{11}H_{13}O_2N$. Calculated %: N 7.33.

0.2 g of the 5-amino-ac-tetrahydro-1-naphthoic acid prepared in this experiment was heated to 80° for 3 hours with 0.5 ml of acetic anhydride and 1 ml of ethyl acetate. The precipitated acetyl derivative was filtered out and washed with ethyl acetate, m.p. 227-229°. Recrystallization from aqueous alcohol raised the m.p. of the substance to 230-231° (with decomposition). Its mixed melting point with the 5-acetamino-ac-tetrahydro-1-naphthoic acid we had synthesized earlier was 232° (with decomposition).

6.570 mg substance: 0.363 ml N_2 (21.5°, 734.5 mm). 3.607 mg substance: 8.858 mg CO_2; 2.052 mg H_2O. Found %: C 66.97; H 6.36; N 6.19. $C_{13}H_{15}O_3N$. Calculated %: C 66.96; H 6.44; N 6.01.

Ethyl ester of 5-amino-ac-tetrahydro-1-naphthoic acid. 1.3 g of 5-amino-ac-tetrahydro-1-naphthoic acid was heated to boiling for 6 hours with 30 ml of absolute ethyl alcohol and 0.6 ml of concentrated sulfuric acid. The alcohol was driven off, and the residue was treated with 10% soda solution and then extracted with ether. The ether extract was washed with soda and then with water and dried over anhydrous sodium sulfate. Driving off the ether left behind 1 g of a yellowish mass, which was distilled in vacuo.

The ethyl ester of 5-amino-ac-tetrahydro-1-naphthoic acid was a highly viscous oil, colorless and odorless, with a b.p. of 160° at 3 mm; $n_D^{19.5}$ 1.5604.

6.845 mg substance: 0.380 ml N_2 (22.0°, 747.0 mm). 17.50 mg substance: 0.954 ml N_2 (19.0° 745.0 mm). Found %: N 6.31, 6.25. $C_{13}H_{17}O_2N$. Calculated %: N 6.39.

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[1] Ekstrand [3] had previously synthesized 5-amino-1-naphthoic acid by reducing 5-nitro-1-naphthoic acid with $FeSO_4$ in ammonia. We also synthesized 5-amino-1-naphthoic acid from 5-nitro-1-naphthoic acid, but by a catalytic method. We used 6.5 g of 5-nitro-1-naphthoic acid, 300 ml of ethyl alcohol, and 20 g of Ni catalyst (Raney's) in the reaction. Hydrogenation was performed at 30-40°. Absorption of the requisite quantity of hydrogen and the customary processing yielded a yellowish substance with an m.p. of approximately 200°, which was impure 5-amino-1-naphthoic acid. The substance was not further refined.

Diethylaminoethyl ester of 5-amino-ac-tetrahydro-1-naphthoic acid (hydrochloride). 6 grams of Raney's nickel catalyst was added to a solution of 1.4 g of the hydrochloride of the diethylaminoethyl ester of 5-nitro-ac-tetrahydro-1-naphthoic acid in 20 ml of absolute ethyl alcohol, and the mixture was agitated in a hydrogen atmosphere. When the reaction was over, the catalyst was filtered out, and the alcohol was driven off in vacuum. 3-4 ml of absolute alcohol and 80 ml of absolute ether were added to the residue.

Rubbing with a glass rod yielded 0.75 g of a colorless crystalline substance with an m.p. of 131-132°. The hydrochloride of the diethylaminoethyl ester of 5-amino-ac-tetrahydro-1-naphthoic acid was nonhygroscopic, soluble in water, alcohol, acetone, and chloroform, and insoluble in toluene, ethyl acetate, and CCl_4.

7.685 mg substance: 0.569 ml N_2 (21.5°, 737.0 mm). 6.040 mg substance: 0.454 ml N_2 (21.0°, 745.0 mm). Found %: N 8.32, 8.56. $C_{17}H_{26}O_2N_2 \cdot HCl$. Calculated %: N 8.58.

7-Amino-ac-tetrahydro-1-naphthoic acid. 6.63 grams of 7-nitro-ac-tetrahydro-1-naphthoic acid was dissolved in 150 ml of methanol, and the solution was agitated in a hydrogen atmosphere together with 5 g of Raney's nickel catalyst. The reaction was carried out at 20-25°. After the requisite quantity of hydrogen (2000 ml) had been absorbed, the catalyst was filtered out, and the methanol was driven off in vacuo, the residue being 5.7 g of a colorless crystalline substance with an m.p. of 169-170°. Recrystallization from alcohol raised the m.p. of the 7-amino-ac-tetrahydro-1-naphthoic acid to 170-171°; it was slightly soluble in methanol, ethyl alcohol, and acetone, and insoluble in ether.

6.105 mg substance: 0.386 ml N_2 (21.5°, 738.5 mm). Found %: N 7.12. $C_{11}H_{13}O_2N$. Calculated %: N 7.33.

7-Acetamino-ac-tetrahydro-1-naphthoic acid. 0.5 gram of 7-amino-ac-tetrahydro-1-naphthoic acid was heated to 80° for 3 hours with 0.8 ml of acetic anhydride. 1 ml of glacial acetic acid was added, and when the mixture had cooled, the precipitated acetyl derivative was filtered out.

7-Acetamino-ac-tetrahydro-1-naphthoic acid had an m.p. of 186-187° after repeated recrystallization from aqueous alcohol; it was a colorless substance that was soluble in alcohol and insoluble in ethyl acetate.

4.978 mg substance: 0.268 ml N_2 (19.0°, 729.0 mm). Found %: N 6.04. $C_{13}H_{15}O_3N$. Calculated %: N 6.01.

Ethyl ester of 7-amino-ac-tetrahydro-1-naphthoic acid. 3.0 g of 7-amino-ac-tetrahydro-1-naphthoic acid was heated to boiling for 7 hours with 40 ml of absolute ethyl alcohol and an adequate quantity of concentrated H_2SO_4 (until its reaction was acid with Congo red).

Processing that was identical with that described above for the 5-amino acid yielded the ethyl ester of 7-amino-ac-tetrahydro-1-naphthoic acid as a wholly colorless and odorless, highly viscous oil with a b.p. of 159.5-160° at 2.5 mm; $n_D^{18.5}$ 1.5580.

12.285 mg substance: 0.687 ml N_2 (18.0°, 740.5 mm). 9.225 mg substance: 0.539 ml N_2 (18.0°, 740.5 mm). Found %: N 6.39, 6.67. $C_{13}H_{17}O_2N$. Calculated %: N 6.39.

Decarboxylation of 7-amino-ac-tetrahydro-1-naphthoic acid. 5 grams of 7-amino-ac-tetrahydro-1-naphthoic acid was thoroughly triturated with 10 g of $Ba(OH)_2$ and a small amount of methanol. The mixture was dried, pulverized, and destructively distilled from a Wurtz flask at 20-30 mm pressure. The distillate was extracted with ether, and the ether solution was washed with a potassium hydroxide solution and dried with potassium hydroxide. The ether was driven off, and the residue (2 g) distilled at ordinary pressure, b.p. 270-275°; the substance quickly crystallized after distillation, m.p. 40-45°.

Repeated recrystallization from petroleum ether yielded a minute quantity of a substance with an m.p. of 104-106° that was slightly soluble in petroleum ether and a more highly soluble substance with an m.p. of 38-39°. The melting point of the substance with an m.p. of 38-39° indicated that it was ar-tetrahydro-2-naphthylamine [4] – colorless needles that crystallized from petroleum ether only after deep chilling.

6.900 mg substance: 0.596 ml N_2 (22.0°, 736.0 mm). Found %: N 9.68. $C_{10}H_{13}N$. Calculated %: N 9.52.

The acetyl derivative was prepared by reacting an ether solution of ar-tetrahydro-2-naphthylamine with acetyl chloride in the presence of sodium carbonate. Needles with an m.p. of 105.5-106.5° [5].

8.101 mg substance: 0.522 ml N_2 (23.0°, 736.0 mm). Found %: N 7.20. $C_{12}H_{15}ON$. Calculated %: N 7.40.

The substance with an m.p. of 104-106° referred to above was not refined further owing to the minute quantity available; it apparently was somewhat impure 2-naphthylamine. Its mixed melting point with pure

2-naphthylamine (m.p. 110°) was 106-108°.

Diethylaminoethyl ester of 7-amino-ac-tetrahydro-1-naphthoic acid (hydrochloride). The hydrochloride of the diethylaminoethyl ester of 7-nitro-ac-tetrahydro-1-naphthoic acid was reduced under the same conditions as those used in reducing the hydrochloride of the alkamino ester of 5-nitro-ac-tetrahydro-1-naphthoic acid. 2.6 grams of the alkamino ester of the 7-nitro acid yielded 1.5 g of the alkamino ester of the 7-amino acid.

The hydrochloride of the diethylaminoethyl ester of 7-amino-ac-tetrahydro-1-naphthoic acid consisted of beautiful, minute needles with an m.p. of 113-116° (with slight decomposition). The substance was nonhygroscopic, freely soluble in water, alcohol, acetone, and chloroform, and insoluble in ethyl acetate, ether, and CCl_4.

6.205 mg substance: 0.460 ml N_2 (20.5°, 738.0 mm). 5.925 mg substance: 0.441 ml N_2 (24.5°, 740.0 mm). Found %: N 8.38, 8.31. $C_{17}H_{26}O_2N_2 \cdot HCl$. Calculated %: N 8.58.

5,7-Dinitro-ac-tetrahydro-1-naphthoic acid. a) 13 grams of the ac-tetrahydro-1-naphthoic acid was gradually added to 75 ml of HNO_3 (sp. gr. 1.5), the temperature being kept at 17-20°. The reaction mixture was allowed to stand at room temperature for 40 minutes and then poured over ice. The white precipitate was filtered out the next day. This yielded 18 g of a substance with an m.p. of 158-160°. The yield of the impure dinitro acid was 92% of the theoretical. Recrystallization from toluene yielded 15 g of a substance with an m.p. of 162-164°.

The 5,7-dinitro-ac-tetrahydro-1-naphthoic acid had an m.p. of 167.5-168.5° after having been purified by conversion into an ester and saponification of the latter. Crystals with a greenish tinge, soluble in acetone, ether, and acetic acid, sparingly soluble in cold toluene and in chloroform.

6.105 mg substance: 0.579 ml N_2 (18.0°, 732.5 mm). 3.132 mg substance: 5.709 mg CO_2. 1.062 mg H_2O. 4.240 mg substance: 7.715 mg CO_2: 1.446 mg H_2O. Found %: C 49.71, 49.62; H 3.79, 3.82; N 10.73. $C_{11}H_{10}O_6N_2$. Calculated %: C 49.62; H 3.77; N 10.52.

b) 0.5 gram of 5-nitro-ac-tetrahydro-1-naphthoic acid was placed in 10 ml of HNO_3, sp. gr. 1.50. The temperature was kept at +20°. Nitration lasted 15 minutes, after which the reaction mixture was poured over ice (about 50 mg of ice). The next day the dinitro acid precipitate was filtered out, m.p. 164-165.5°. Several recrystallizations from toluene yielded 5,7-dinitro-ac-tetrahydro-1-naphthoic acid with an m.p. of 167-167.5°. Its mixed melting point with the 5,7-dinitro-ac-tetrahydro-1-naphthoic acid described above (see the preceding experiment) was 167-168°.

6.185 mg substance: 0.578 ml N_2 (20.0°, 714.5 mm). Found %: N 10.25. $C_{11}H_{10}O_6N_2$. Calculated %: 10.52.

c) 1.1 grams of 7-nitro-ac-tetrahydro-1-naphthoic acid was placed in 10 ml of HNO_3, sp. gr. 1.50. The reaction lasted 15 minutes at room temperature. The customary processing yielded 1.2 g of a substance with an m.p. of 165-167°. After recrystallization from toluene raised the m.p. of the substance to 167-167.5°; it was 5,7-dinitro-ac-tetrahydro-1-naphthoic acid. Its mixed melting point with the 5,7-dinitro-ac-tetrahydro-1-naphthoic acid described above was 167-167.5°.

7.260 mg substance: 0.658 ml N_2 (20.0°, 737.0 mm). Found %: N 10.24. $C_{11}H_{10}O_6N_2$. Calculated %: N 10.52.

Oxidation of 5,7-dinitro-ac-tetrahydro-1-naphthoic acid. 0.7 gram of 5,7-dinitro-ac-tetrahydro-1-naphthoic acid was heated to 145-150° with 16 ml of 40% HNO_3 in a sealed tube for 8 hours. When the reaction was over, the acid solution was evaporated to dryness on a water bath. The residue was a grayish substance that was freely soluble in water and had an m.p. of approximately 210° (with decomposition). The yield was 0.6 g. Several recrystallizations from an ether-ligroin mixture raised the m.p. of the substance to 223-224° (with decomposition). The melting point and analysis of the synthesized substance indicated that it was the 3,5-dinitophthalic acid described in the literature [6].

5.09 mg substance: 0.477 ml N_2 (22.5°, 750.0 mm). 5.205 mg substance: 0.488 ml N_2 (22.5° 750.0 mm). Found %: N 10.70, 10.70. $C_8H_4O_8N_2$. Calculated %: N 10.94.

The monoethyl ester of 3,5-dinitrophthalic acid was prepared as specified by Beilstein and Kurbatov [6]. 0.25 gram of the 3,5-dinitrophthalic acid we had prepared by oxidizing dinitrotetrahydronaphthoic acid was heated with a small amount of absolute ethyl alcohol that contained anhydrous hydrogen chloride. Heating lasted 5 hours, after which the alcohol was driven off in vacuo. Water was added to the residue, and the precipitate was filtered out, yielding 0.2 g of the monoethyl ester of 3,5-dinitrophthalic acid, with an m.p. of 184.5°. Recrystallization from a chloroform-petroleum ether mixture raised the melting point to 185-186°.

Ethyl ester of 5,7-dinitro-ac-tetrahydro-1-naphthoic acid. 22 grams of 5,7-dinitro-ac-tetrahydro-1-naphthoic acid was heated to boiling for 8 hours with 250 ml of absolute ethyl alcohol and 5 ml of concentrated sulfuric acid. After the reaction most of the alcohol was driven off, about 50 ml of water was added to the residue, and the ethyl ester of the dinitro acid that separated out was extracted with ether. The ether solution was washed with a 10% soda-solution and then with water. It was dried over anhydrous sodium sulfate, after which the ether was driven off, and the residue recrystallized twice from absolute ethyl alcohol. This yielded 18 g of a colorless substance with an m.p. of 43.5-44.5°, which was readily soluble in ether, benzene, and hot alcohol and sparingly soluble in cold alcohol and in petroleum ether.

7.800 mg substance: 0.680 ml N_2 (21.5°, 738.0 mm). Found %: N 9.85. $C_{13}H_{14}O_6N_2$. Calculated %: N 9.52.

5,7-Dinitro-ac-tetrahydro-1-naphthoyl chloride. 6 grams of 5,7-dinitro-ac-tetrahydro-1-naphthoic acid was heated for 2 hours with 10 ml of thionyl chloride. The excess thionyl chloride was driven off in vacuo, and some petroleum ether was added to the residue. After the solution had cooled, rubbing threw down a white precipitate. The precipitate was filtered out and washed with petroleum ether. This yielded 6 g of a substance with an m.p. of 88-90°.

The 5,7-dinitro-ac-tetrahydro-1-naphthoyl chloride has an m.p. of 89.5-90.5° after recrystallization from a benzene-petroleum ether mixture. Rather freely soluble in benzene, sparingly in ether and petroleum ether.

0.1588 g substance: 0.0831 g AgCl. Found %: Cl 12.94. $C_{11}H_9O_5N_2Cl$. Calculated %: Cl 12.48.

5,7-Diamino-ac-tetrahydro-1-naphthoic acid. 5,7-Dinitro-ac-tetrahydro-1-naphthoic acid was dissolved in 450 ml of methanol. 10 grams of Raney's nickel catalyst was added to the solution, and the mixture was agitated in a hydrogen atmosphere; after the requisite quantity of hydrogen (3860 ml) had been added, the catalyst was filtered out, and the methanol driven off in vacuo; hydrogen or some other inert gas has to be passed through a capillary while the methanol is being driven off in vacuo. This yielded 4.7 g of a brown substance with an m.p. of 172° (with decomposition). The yield was 81% of the theoretical.

After recrystallization from absolute ethyl alcohol the 5,7-diamino-ac-tetrahydro-1-naphthoic acid had an m.p. of 177° (wtih decomposition). Light-yellow crystals, somewhat soluble when heated in methanol or ethyl alcohol, sparingly soluble in the alcohols or in ethyl acetate at room temperature. The alcoholic solutions were oxidized extremely readily by atmospheric oxygen.

5.470 mg substance: 0.660 ml N_2 (20.5°, 733.0 mm). 5.570 mg substance: 0.676 ml N_2 (19.5° 732.0 mm). Found %: N 13.55, 13.64. $C_{11}H_{14}O_2N_2$. Calculated %: N 13.59.

5,7-Diacetamino-ac-tetrahydro-1-naphthoic acid. 0.5 gram of 5,7-diamino-ac-tetrahydro-1-naphthoic acid was heated to 70-80° for 3 hours with 1 ml of acetic anhydride. The reaction mass was treated with water, throwing down a colorless precipitate of the acetyl derivative. This yielded 0.5 g of a substance with an m.p. of 207-210°.

After recrystallization from aqueous alcohol the 5,7-diacetamino-ac-tetrahydro-1-naphthoic acid consisted of colorless needles with an m.p. of 211.5-212.5° that were readily soluble in alcohol.

6.400 mg substance: 0.550 ml N_2 (20.5°, 733.0 mm). 6.900 mg substance: 0.590 ml N_2 (19.5°, 732.0 mm). Found %: N 9.65, 9.51. $C_{15}H_{18}O_4N_2$. Calculated %: N 9.65.

Decarboxylation of 5,7-diamino-ac-tetrahydro-1-naphthoic acid. A mixture of 2.0 g of 5,7-diamino-ac-tetrahydro-1-naphthoic acid and 4.5 g of Ba $(OH)_2$ was distilled destructively in vacuo (5-15 mm pressure). This yielded about 1 g of a substance that was dissolved in ether, the ether solution being washed with an alkali solution and dried over anhydrous sodium sulfate. The ether was driven off, and the residue (m.p. 73-75°) recrystallized twice from absolute ether, which raised the substance's melting point to 79.5-80°. This is the melting point of ar-1,3-tetrahydronaphthalenediamine [7].

4.04 mg substance: 0.606 ml N_2 (21.5°, 752.0 mm). Found %: N 17.20. $C_{10}H_{14}N_2$. Calculated %: N 17.28.

5-Nitro-ac-tetrahydro-1-thionaphthoic acid. A solution of 4.3 grams of KOH in 40 ml of absolute alcohol was saturated with hydrogen sulfide at -5°. A solution of 7.4 g of 5-nitro-ac-tetrahydro-1-naphthoylchloride in 30-35 ml of absolute benzene was gradually added, during the course of 15 minutes, to the resulting solution of KSH. The reaction was carried out with vigorous stirring at -5 to -2°. Fifteen minutes later the precipitated KCl was filtered out, the solvent driven off in vacuo, and the residue triturated with absolute ether. The precipitated potassium salt of the thio acid was filtered out and dried in vacuo, yielding 7 g of the substance. 0.5 g of the potassium salt of the thio acid was dissolved in 5 ml of water, and the solution was filtered and acidified with dilute hydrochloric acid. The oil that separated out crystallized rapidly into a solid, nearly colorless substance with an m.p. of 69°.

After recrystallization from alcohol the 5-nitro-ac-tetrahydro-1-thionaphthoic acid was a yellowish crystalline substance with an m.p. of 69.5-70.5°, which was readily soluble in ether and hot alcohol, and sparingly soluble in cold alcohol and water.

0.1330 g substance: 0.1310 g $BaSO_4$. 0.1225 g substance: 0.1195 g $BaSO_4$. Found %: S 13.52, 13.39. $C_{11}H_{11}O_3NS$. Calculated %: S 13.50.

Ethyl ester of 5-nitro-ac-tetrahydro-1-thionaphthoic acid. 5.5 grams of the potassium salt of 5-nitro-ac-tetrahydro-1-thionaphthoic acid was dissolved in 10 ml of absolute ethyl alcohol, about 5 ml of ethyl iodide was added to the solution, and the mixture was heated for an hour on a water bath at 60-70°. After all the KI had been precipitated, the solution was treated with water and extracted with ether. The ether extract was dried over anhydrous sodium sulfate, after which the ether was driven off and the residue distilled in vacuo.

This yielded 4 g of the ethyl ester of 5-nitro-ac-tetrahydro-1-thionaphthoic acid — a yellowish oil with a b.p. of 175-176° at 1-1.5 mm, which crystallized in the cold.

0.2455 g substance: 0.2221 g $BaSO_4$. Found %: S 12.42. $C_{13}H_{15}O_3NS$. Calculated %: S 12.07.

7-Nitro-ac-tetrahydro-1-thionaphthoic acid. This was synthesized like the 5-nitro-ac-tetrahydro-1-thionaphthoic acid. A solution of 8 g of the acid chloride of the 7-nitro acid in absolute benzene was added to an alcoholic solution of potassium hydrosulfide (produced by saturating 4.3 g of potassium hydroxide with hydrogen sulfide). Appropriate processing yielded 7 g of the potassium salt of the 7-nitro thio acid.

The 7-nitro-ac-tetrahydro-1-thionaphthoic acid crystallized excellently from alcohol as a yellowish crystalline substance with an m.p. of 74.5-75.5°, which was soluble in ether, benzene, hot alcohol and CCl_4, and somewhat soluble in cold alcohol.

0.1749 g substance: 0.1701 g $BaSO_4$. 0.1716 g substance: 0.1665 g $BaSO_4$. Found %: S 13.35, 13.32. $C_{11}H_{11}O_3NS$. Calculated %: S 13.50.

Ethyl ester of 7-nitro-ac-tetrahydro-1-thionaphthoic acid. This was synthesized, like the 5-nitro isomer, by reacting an alcoholic solution of the potassium salt of the 7-nitro thio acid with ethyl iodide. The ethyl ester of 7-nitro-ac-tetrahydro-1-thionaphthoic acid was a light-yellow oil with a b.p. of 184° at 2-2.5 mm. It could be crystallized in the cold.

0.1791 g substance: 0.1560 g $BaSO_4$. Found %: S 11.96. $C_{13}H_{15}O_3NS$. Calculated %: S 12.07.

Diethylaminoethyl ester of 7-nitro-ac-tetrahydro-1-thionaphthoic acid (hydrochloride). 3.2 grams of the potassium salt of 7-nitro-ac-tetrahydro-1-thionaphthoic acid was dissolved in 40 ml of absolute ethyl alcohol, 1.71 g of the hydrochloride of diethylamino-ethyl chloride was added to the solution, and the mixture was heated to 60-70° for 4 hours. The precipitated potassium chloride was filtered out, and the alcohol was then driven off in vacuo. The residue was treated with a 10% soda solution, and the base of the alkamino ester was extracted with ether. The ether solution was dried over anhydrous sodium sulfate, and a solution of hydrogen chloride in absolute ether was added, throwing down the hydrochloride of the alkamino ester. This yielded 3.3 g of a substance with an m.p. of 144-147°.

Reprecipitation from alcohol by ether yielded the hydrochloride of the diethylaminoethyl ester of 7-nitro-ac-tetrahydro-1-thionaphthoic acid as a coloress, nonhygroscopic substance with an m.p. of 147.5-149°, soluble in water and alcohol, and insoluble in ether.

0.1060 g substance: 0.0653 g $BaSO_4$. 5.710 mg substance: 0.400 ml N_2 (19.5°, 724.0 mm). Found %: S 8.46; N 7.80. $C_{17}H_{24}O_3N_2S \cdot HCl$. Calculated %: S 8.59; N 7.51.

SUMMARY

1. Nitrating ac-1-tetrahydronaphthoic acid with nitric acid, sp. gr. 1.5, yields 5,7-dinitro-(1,2,3,4-tetrahydro)-1-naphthoic acid, while nitration with nitric acid, sp.gr. 1.4, yields a mixture of two mononitro acids: 5- and 7-nitro-(1,2,3,4-tetrahydro)-1-naphthoic acid; a method is set forth for separating these mononitro acids.

2. The structure of the synthesized nitro acids is established by converting them into compounds of known structure.

3. Catalytic reduction is employed to secure the respective diamino and amino-ac-1-tetrahydronaphthoic acids from the dinitro and mononitrotetrahydronaphthoic acids.

4. The simplest derivatives of all the nitro (amino)-ac-1-tetrahydronaphthoic acids have been synthesized.

5. 5 (7)-Nitro-ac-1-tetrahydrothionaphthoic acids and some of their derivatives have been synthesized.

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Received November 4, 1950.

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* See Consultants Bureau translation, p. 109.

THE ALKALOIDS OF THALICTRUM MINUS L.

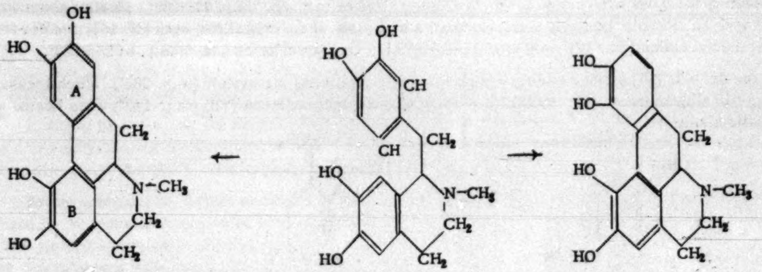
II. THE STRUCTURE OF THALICMIDINE AND THALICMINE

S. Yunusov and N. N. Progressov

We have already reported [1] that in our investigation of the above-ground parts of Thalictrum minus L. we succeeded in isolating two alkalids (thalmine and thalmidine), while the roots of this plant yielded three bases (thalicmine, thalicmidine, and Base No. 5). Thus we have secured five new alkaloids in crystalline form from the whole of the plant Thalictrum minus L. Some of the physicochemical properties were given for four of the alkaloids, together with their incomplete structural formulas. These findings led us to postulate that these alkaloids are derivatives of tetrahydroisoquinoline.

In the course of further research on thalicmidine we were able to confirm this hypothesis experimentally and to establish conclusively that aporphine is the parent substance of this alkaloid. Now, this base contains two less hydrogen atoms than was reported earlier [1], i.e., thalicmidine is $C_{20}H_{23}NO_4$. What we still had to determine was the function of the fourth oxygen atom. We found that this oxygen atom possesses weak phenolic properties, inasmuch as thalicmidine dissolves in dilute alkalies and is extracted from alkaline solution completely by ether; diazomethane does not methylate it even when used in considerable excess. Hence, the formula of thalicmidine may be depicted as $C_{16}H_{10}(NCH_3)(OH)(OCH_3)_3$. Reaction with acetic anhydride yields an optically inactive substance that has no basic properties, which we oxidized with nitric acid (sp. gr. 1.34). This reaction yielded mellophanic acid, as was confirmed by securing the crystalline tetramethyl ester of that acid. All the foregoing reactions lead to the conclusion that the basic skeleton of thalicmidine is aporphine.

The one thing that was left to establish the structure of thalicmidine was fixing the position of the substituent groups. As we know, all tetrasubstituted aporphine alkaloids known up to the present are derivatives of two types of tetrahydroxyaporphine (I and II).



(I) (II)

One of the present authors has discovered some general properties of alkaloids of the aporphine group that facilitate determination of the position of the substituent groups.

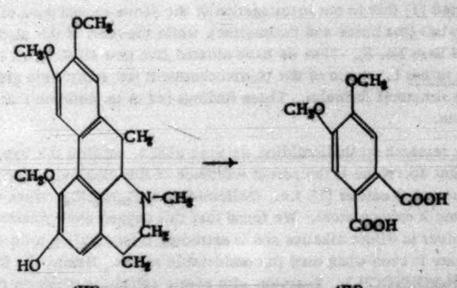
1. No mellophanic acid is produced when the product of the action of acetic anhydride upon alkaloids that have no substitutents in the A and B benzene rings is oxidized with strong nitric acid. Instead, benzenedi- or tricarboxylic acid is produced, depending upon the positions of the substitutents in one of these rings.

2. Alkaloids that are aporphine derivatives possessing substituent groups at the 2,3,5,6 and 3,5,6 positions have a specific rotatory power (40-100°) that is much smaller than that of bases having substituents at the 3,4,5,6 and 4,5,6 position (200-300°).

3. This group is almost always located at the 5 and 6 positions in all aporphine alkaloids that contain a methylenedioxy group.

4. Hydroxyl groups at the 5 and 6 positions are weakly phenolic.

Inasmuch as the $[\alpha]_D - 84.05°$, the hydroxyl group is weakly phenolic, and oxidation yields mellophanic acid, the foregoing rules indicate that thalicmidine must have the structure (III) [3]:

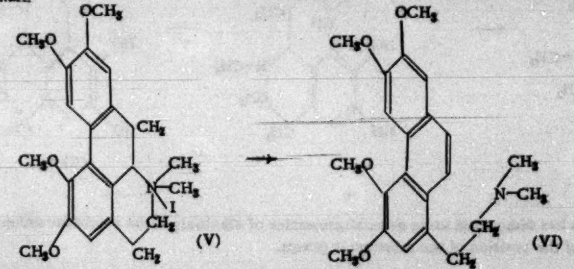


(III) (IV)

The fact that we secured metahemipinic acid (IV) by oxidizing thalicmidine with potassium permanganate is partial confirmation of this structure. It follows that the two methoxy groups occupy the 2 and 3 positions.

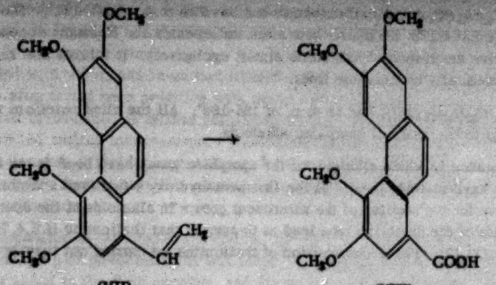
We secured further experimental evidence in support of the correctness of the formula (III) by carrying out a Hofmann decomposition of the methyl ester of thalicmidine. After finding that we could not methylate the hydroxyl group of thalicmidine with diazomethane, we secured the methiodide of the methyl ester of thalicmidine (V) by reacting the latter with methyl iodide in a dilute alkaline medium. M.p. 221-222°. Heating the methiodie (V) with an alcoholic (methyl) alkali produced a high yield of the crystalline, optically inactive des-N-methyl-O-methylthalicmidine (VI) with an m.p. of 72-73.5°. Its hydrochloride had an m.p. of 255-257°.

The des-base (VI) yields an easily and excellently crystallizing methiodide (m.p. 280°), which breaks down into trimethylamine and the crystalline tetramethoxyvinylphenanthrene (VII) (m.p. 143°) when heated with an alcoholic alkali:

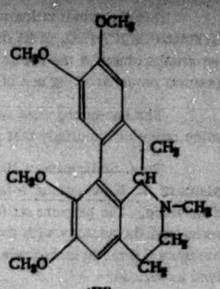


(V) (VI)

When the non-nitrogenous substance (VII) was oxidized with potassium permanganate in acetone solution, we obtained the corresponding crystalline monocarboxylic acid (VIII), with an m.p. of 218°. It follows that the only possible structure for the methyl ester of thalicmidine is (IX):



(VII) (VIII)



(IX)

The properties and formula of methylthalicmidine (IX) established by us agree almost completely with the properties of glaucine (IX) [4], O-dimethylboldine (IX) [5], and their derivative and decomposition products (see the table):

TABLE

Name of substance	O-Methylthalicmidine	Glaucine	O-Dimethylboldine
Methiodidide	221-222°	222°	221°
Methiodide of the des-bas	276-280	278-280	276-280
Tetramethoxyvinylphenanthrene	143	142	143
Tetramethoxyphenanthrenecarboxylic acid	218		214

For want of glaucine or boldine, we were unable to identify them conclusively immediately. But all the facts cited above prove that O-methylthalicmidine (IX) is identical with glaucine and O-dimethylboldine. On the basis of certain phylogenetic considerations set forth by one of the present authors in his article entitled "The dynamics of the accumulation, the role, and the formation of alkaloids in plants" [6], we assumed that Thalictrum minus L. must contain O-methylthalicmidine, i.e., glaucine, depending upon its period of growth and habitat. As a matter of fact, glaucine has been isolated from the nonphenolic portion of the alkaloids obtained from the roots of Thalictrum minus L. gathered (on May 23-28, 1949) in the stage of unripe fruit (in Kuyan-sae, Kulsu landmark, Zaamink District, Uzbek S.S.R.). We have thus been able to confirm the formula for O-methylthalicmidine (IX) conclusively by making direct determinations of the mixed melting points of their methiodides and des-products.

It should be noted that the Hofmann decomposition of thalicmidine and of its methyl ester normally takes place along only one of the theoretically possible lines, yielding the crystalline, optically inactive des-N-methylthalicmidine (m.p. 252-253°). The hydroxyl group retained in the last substance is likewise weakly phenolic.

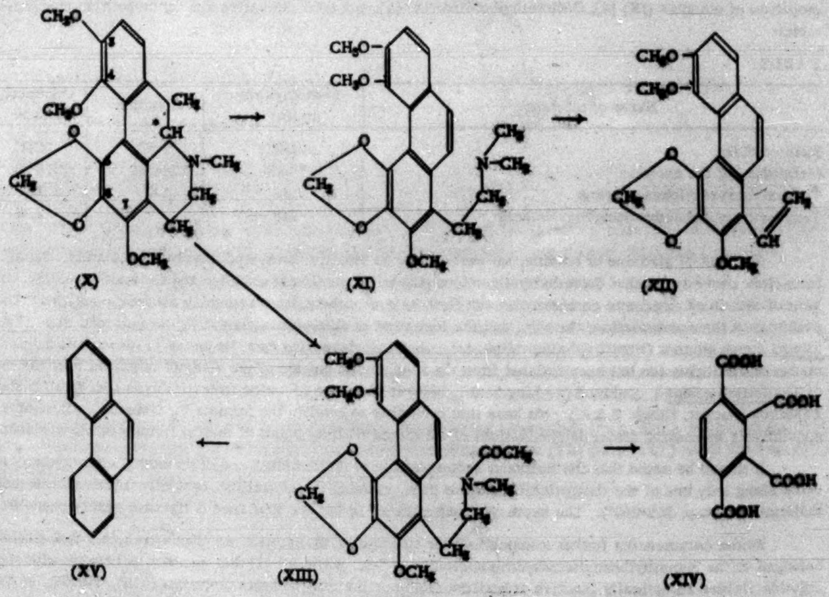
Before commencing further research into the structure of thalicmine, we checked whether that alkaloid belonged to the N-methylbenzyltetrahydroisoquinoline series. We found [1] that reacting thalicmine with acetyl chloride yielded an optically inactive crystalline substance that had no basic properties (XIII). Further, by oxidizing this substance with strong nitric acid we obtained the tetracarboxylic acid (XIV), whose mixed melting point with mellophanic acid, as well as that of their tetramethyl esters, exhibited no depression. Moreover, by distilling the synthesized optically inactive monoacetylthalicmine with zinc dust, we isolated an adequate percentage of phenanthrene (XV) from the reaction products. These reactions clearly show that thalicmine does not belong to the benzyltetrahydroisoquinoline series, but rather to a related one, the aporphine series. Hence the amount of hydrogen it contains, which is hard to determine from the analytical data, becomes clear: the composition of thalicmine is $C_{21}H_{23}NO_5$.

Thalicmine is a tertiary base that contains an NCH_3 group. Three oxygen atoms are contained in methoxy groups, the two others being in a methylenedioxy group: $C_{16}H_8(NCH_3)(OCH_3)_3(CH_2O_2)$. Thalicmine is decomposed readily and smoothly in a Hofmann reaction. Repeating the decomposition twice by reacting the methiodide with a 30 % KOH solution in methanol yields trimethylamine and a nonnitrogenous substance.

Des-N-methylthalicmine (XI) C$_{22}$H$_{25}$NO$_5$ is optically inactive and have an m.p. of 150-151°. The m.p. of its sulfate is 127-128°, of its methiodide 236-237°. No matter how often we repeated the Hofmann decomposition we always obtained the optically inactive des-N-methylthalicmine almost exclusively. It follows that the decomposition proceeds along one of the theoretically conceivable lines.

The non-nitrogenous substance, C$_{20}$H$_{18}$O$_5$ (XII), had an m.p. of 185-186°. All the cited reactions with thalicmine prove convincingly that it belongs to the series of aporphine alkaloids.

Thus, thalicmine is the first instance in which alkaloids of the aporphine group have been found in the plants of the Ranunculaceae family we have studied, as well as the first pentahydroxy substituted aporphine ever discovered. The patterns set forth above for the position of the substituent groups in alkaloids of the aporphine series and the analogy with the alkaloids of the narcotine type lead us to assume that thalicmine is 3,4,7-trimethoxy-5,6-methylenedioxyaporphine (X) [3]. The decomposition of thalicmine we carried out may be summarized as follows:



(X) (XI) (XII)

(XV) (XIII) (XIV)

EXPERIMENTAL

Mellophanic acid from thalicmidine. 1.2 grams of thalicmidine was dissolved in 7 ml of acetic anhydride and boiled for one hour. After all the anhydride and acetic acid had been evaporated in a dish on a water bath, what was left was a noncrystalline mass that exhibited no basicity or optical activity. The residue was evaporated 5 times with 8 ml portions of nitric acid (sp. gr. 1.34) on a water bath. The resultant yellow amorphous residue was recrystallized from strong nitric acid. The crystalline acid, with an m.p. of 233-236°, exhibited no depression of the melting point when mixed with the mellophanic acid secured from thebaine. Nor did the mixed melting point (134°) of the tetramethyl esters of these acids, prepared by methylating them with diazomethane, exhibit any depression.

Oxidation of thalicmidine. 1.3 grams of the base, with an m.p. of 192-193°, was dissolved in 15 ml of 2% hydrochloric acid. Then the solution was neutralized and stirred mechanically while a 3% solution of KMnO$_4$

(9.9 g in 300 ml of water) was added. The whole of the permanganate solution (24 atoms of oxygen) was added in the space of two hours. Then the solution was heated to 40° for one hour. The unreacted permanganate was decolorized by adding pulverized Na_2SO_3. The solution was filtered, the manganese dioxide being transferred to a flask, boiled with water, and re-suction-filtered. The filtrates (500 ml) were combined. The solution was extracted with ether after it had been acidified with strong hydrochloric acid. After it had been dried and the ether driven off, the mass crystallized as minute yellow-orange needles. The yield was 0.8 g. Dissolving in alcohol and adding freshly distilled aniline instantaneously yielded the anilide with an m.p. of 168-169°. The m.p. was raised to 170-171° (with decomposition) by recrystallization from absolute alcohol. Its mixed melting point with metahemipinanilide, prepared from salsolidine, exhibited no depression, all three samples fusing simultaneously at 170-171° (with decomposition).

Methiodide of O-methylthalicmidine. 20 ml of methanol was poured over 2 g of thalicmidine ground to a powder, and 0.4 g of powdered KOH was added. The whole dissolved, the solution turning dark. 1 ml of methyl iodide was added to the flask contents, and the mixture was refluxed one hour. After the contents had cooled, another 1 ml of methyl iodide was added, the mixture was again refluxed for 2 hours and left to stand for 14 hours. Crystals settled out of the methanol partially. The solution was neutralized with litmus paper. The solvent was evaporated to a volume of 10 ml, which increased the quantity of crystals, the whole mass crystallizing when a rod was used for rubbing. The crystals were suction-filtered and washed with methanol. Recrystallization from water yielded minute acicular crystals with an m.p. of 221-222°. The yield was 2.2 g.

Des-O-methyl-N-methylthalicmidine. 2.2 grams of the methioidide of O-methylthalicmidine was ground to a powder and transferred to a flask that contained 25 ml of 30% KOH (7.5 g) in methyl alcohol. After the mixture had been boiled for 3 hours, the methanol was driven off, and evaporation was continued in a dish. The adding of water caused a yellow resinous mass of the des-base to float to the surface; it was separated and washed with water. The des-base, purified via its hydrochloride, consisted of lustrous silvery crystals with an m.p. of 255-257°. 1.4 grams of the hydrochloride of the des-base was dissolved in 100 ml of water and decomposed with 20% ammonia. This yielded the des-base as crystalline flocs (when less water was used, an oily mass settled out, which solidified upon standing). The m.p. was 72-73.5° after suction-filtering, washing with water, and drying, while the oily portion yielded a product with an m.p. of 69-71°. The m.p. was 72-73.5° after recrystallization from petroleum ether (b.p. 60-80°).

0.0224 g substance: 13.3 ml 0.1 N $Na_2S_2O_3$. 0.0230 g substance: 14.4 ml 0.1 N $Na_2S_2O_3$.
Found %: OCH_3 31.31, 33.01. $C_{22}H_{27}NO_4$. Calculated %: OCH_3 33.33.

Methiodide of des-O-methyl-N-methylthalicmidine. 0.6 gram of des-O-methyl-N-thalicmidine, with an m.p. of 72-73.5°, was dissolved in 20 ml of acetone, and 1 ml of methyl iodide was added to the solution. The crystals of the methiodide settled out at once. After standing for an hour they were suction-filtered and washed with acetone. This yielded 0.7 g of snow-white methiodide with an m.p. of 271-274°, slightly soluble in water. The m.p. was raised to 276-280° (with decomposition) by recrystallization from alcohol.

2,3,5,6-Tetramethoxy-8-vinylphenanthrene. 0.7 gram of the methiodide of des-O-methyl-N-methylthalicmidine was ground to a powder and added to a solution of 12.5 ml of 30% KOH (3.75 g) in methanol. The mixture was boiled, trimethylamine being given off and a nonnitrogenous substance being formed. The methanol was evaporated, water was added to the residue, and the product was extracted with ether. The ether solution was washed with 10% sulfuric acid and with water. Drying and driving off the ether yielded crystals of the nonnitrogenous substance with an m.p. of 138-140°. The m.p. was raised to 143° by recrystallization from alcohol. 0.4 g yield.

0.0236 g substance: 18.1 ml 0.1 N $Na_2S_2O_3$. 0.0232 g substance: 16.4 ml 0.1 N $Na_2S_2O_3$.
Found %: OCH_3 40.67, 37.28. $C_{20}H_{20}O_4$. Calculated %: OCH_3 38.27.

2,3,5,6-Tetramethoxyphenanthrene-8-carboxylic acid. 0.2 gram of 2,3,5,6-tetramethoxy-8-vinylphenanthrene was dissolved in 50 ml of acetone and then oxidized with a solution of $KMnO_4$ (0.25 g) in 50 ml of acetone. The permanganate was added in small portions during the course of 2 hours, with constant stirring, to the reaction mass, which was kept at 25°. After all the permanganate had been decolorized, the manganese dioxide was filtered out and washed, first with acetone and then with hot water. After the acetone had been evaporated the mass crystallized in part. The aqueous solution was evaporated on a bath. The mass recovered after the acetone and the water had been driven off was acidified with 10% hydrochloric acid and extracted with ether. The ether solution was washed first with 20 ml of 10% NaOH and then with water, after which the solution was dried and the ether was driven off. The residue was a small quantity of resinous substance. The alkaline solution and the wash waters were acidified with 10% hydrochloric acid and extracted with ether. Drying, followed by driving off the ether, yielded the acid as small crystalline needles with an m.p. of 208°. The m.p. was 218° after recrystallization from alcohol.

Recovery of glaucine. Extracting 43 kg of the roots of Thalictrum minus L., harvested during the unripe fruit stage (July 23-28, 1949), yielded 368.3 g (0.85%) of total ether-soluble alkaloids. 111.2 grams of the technical hydrobromide, with an m.p. of 220-233°, was obtained from an acetone solution of the nonphenolic portion of the total alkaloids, the m.p. being raised to 235-237° by recrystallization from water. Reacting an aqueous solution of 1 g of the hydrobromide (m.p. 235-237°) with 25% ammonia yielded an amorphous base, which soon began to turn yellow. After being washed with water and dried, the base was ground to a powder with an m.p. of 89-90°. After recrystallization from ether, the m.p. was 104-109°; $[\alpha]_D + 84°$.

The methiodide was secured by dissolving 0.8 g of the base in 10 ml of acetone, and adding 1 ml of methyl iodide and refluxing the mixture for 1.5 hours. The finely crystalline methiodide was suction-filtered and washed with acetone. M.p. 216-219°. Yield 0.9 g. Its mixed melting point with crystals of the methiodide of O-methylthalicmidine exhibited no depression.

Performing a Hofmann decomposition reaction under the same conditions as those employed for the O-methyl thalicmidine (30% alcoholic solution of KOH), we secured the des-N-methyl base, with an m.p. of 63-68°, in the first stage. The m.p. was raised to 70-72° by recrystallization from petroleum ether (b.p. 40-60°). The mixed melting point with des-methyl-O-methylthalicmidine exhibited no depression, nor did the mixed melting point of their hydrochlorides(m.p. 256-257°).

The second stage of the Hofmann decomposition reaction was performed with the technical methiodide (m.p. 262-265°). This yielded trimethylamine and a nonnitrogenous crystalline substance with an m.p. of 134-136°. The m.p. was raised to 141-142° by recrystallization from alcohol. The yield was 0.45 g. The mixed melting point with the crystals of the nonnitrogenous product obtained from O-methylthalicmidine exhibited no depression.

Mellophanic acid from Thalicmine. Boiling 1.5 g of thalicmine in 10 ml of acetic anhydride yielded 1.45 g of crystalline N-acetylthalicmine, with an m.p. of 191-192°. This substance was not basic and was optically inactive. Subsequent oxidation with strong nitric acid and identification of the acids and of their esters were effected as in the case of thalicmidine.

Distillation of N-acetylthalicmine with zinc dust. 2.6 grams of N-acetylthalicmine was mixed with 26 g of zinc dust. Then the mixture was wetted with alcohol and sawed into pieces. The mass was dried at 100° and then the pieces were charged into a refractory tube and covered with a layer of asbestos. The tube was placed at a slant in a Liebig electric furnace. Distillation in a current of hydrogen lasted 25 minutes. The contents of the receiver and the tube were washed with ether. The ether solution was washed , first with 30 ml of 10% hydrochloric acid and then with 30 ml of 2% KOH and water, after which it was dried over calcined sodium sulfate. After the ether had been driven off to small volume, the residue was transferred to a small flask, where the phenanthrene partially crystallized. The yield was 0.6 g.

Des-N-methylthalicmine. 2.5 grams of the crystalline methiodide with an m.p. of 235-237° was placed in a flask containing 25 ml of a 30% solution of KOH (7.5 g) in methanol, and the mixture was boiled for 2 hours. Then the solution was driven off. The des-N-methylthalicmine remained insoluble when water was added. The crystals were suction-filtered and washed with water. The aqueous-alkaline solution (orange-colored) was extracted exhaustively with ether. After the ether had been driven off, the crystals produced were combined with the bulk of the crystals of the des-N-methyl base. The yield was 1.7 g, the m.p. 145-149°.

The 1.7 g of the technical des-base was recrystallized from methanol, (1:15). This yielded 1.2 g of minute acicular colorless crystals (flocs), with an m.p. of 150-150.5°. Des-N-methylthalicmine is optically inactive.

0.1242 g substance: 0.3176 g CO_2; 0.0774 g H_2O. 0.1299 g substance: 0.3262 g CO_2; 0.0768 g H_2O. 0.1346 g substance: 0.3395 g CO_2; 0.0820 g H_2O. 0.1106 g substance: 3.8 ml N_2 (19°, 727.92 mm). 0.1134 g substance: 3.9 ml N_2 (17.7°, 733.58 mm). Found %: C 69.23, 68.53, 68.83; H 6.92, 6.61, 6.82; N 3.76, 3.82. $C_{22}H_{25}NO_5$. Calculated %: C 68.93; H 6.52; N 3.65.

Des-N-methylthalicmine sulfate. When the des-base was mixed with 10% sulfuric acid, the sulfate was produced as shiny little lamellae. The m.p. was 127-128° (with decomposition) after recrystallization from water, and 125-127° (with decomposition) from alcohol. The isolated crystalline base had an m.p. of 149-150°.

Des-N-methylthalicmine methiodide. 1.3 gram of des-N-methylthalicmine was dissolved in 20 ml of methanol, and 2.3 g of methyl iodide was added. After a brief period (5 minutes) of gentle heating the crystals of the methiodide were formed, absorbing all the solvent. The mass was boiled for 2 hours and cooled, the crystals being suction-filtered, washed with methanol, and dried. The methiodide consisted of minute acicular, snow-white crystals with an m.p. of 236-237° (with decomposition) in a sealed capillary. The yield was 1.2 g.

The nonnitrogenous product $C_{20}H_{18}O_5$. 9 grams of KOH was dissolved in 30 ml of methanol, 1.7 g of des-N-methylthalicmine methiodide was added to the solution, and the mixture was refluxed. Trimethylamine began to be given off within 15 minutes. The mixture was refluxed for 4 hours. Then the contents of the flask were transferred to a dish and evaporated on a water bath. When water was added, the nonnitrogenous substance floated to the surface as lustrous crystals. The whole mass was transferred to a separatory funnel and extracted with ether. We collected 1 liter of a faintly yellow ether solution. The ether solution was filtered and washed with 25 ml of a 5% solution of hydrochloric acid. The acid solution reacted weakly with silicotungstic acid. The ether solution was rewashed with water, filtered, and dried over sodium sulfate. When the solution was evaporated to a volume of 50 ml, crystals began to settle out of the still-boiling ether as lustrous flakes. The crystals were suction filtered and washed with ether. M.p. 185-186°. The yield was 0.4 g.

0.1224 g substance: 0.3164 g CO_2; 0.0614 g H_2O; 0.1200 g substance: 0.3074 g CO_2; 0.0618 g H_2O. 0.0288 g substance: 12.0 ml 0.1 N $Na_2S_2O_3$; 0.0228 g substance: 12.0 ml 0.1 N $Na_2S_2O_3$. Found %: C 70.54, 71.68; H 5.61, 5.71; OCH_3 27.86, 28.09. $C_{20}H_{18}O_5$. Calculated %: C 70.97; H 5.32; OCH_3 27.51.

SUMMARY

1. Determination of the functional groups has made it possible to portray the formula of thalicmidine, $C_{20}H_{23}NO_4$, as follows: $C_{16}H_{10}(NCH_3)(OCH_3)_3(OH)$; the last hydroxyl group is weakly phenolic. The hydroxyl group retained in des-N-methylthalicmidine is likewise weakly phenolic.

2. Mellophanic acid is formed when the substance obtained from thalicmidine by boiling the latter in acetic anhydride is oxidized. Oxidation of thaicmidine itself yields metahemipinic acid.

3. Repeating the Hofmann decomposition of O-methylthalicmidine twice yields a nonnitrogenous substance, which yields tetramethoxyphenanthrenecarboxylic acid upon oxidation.

4. In the unripe fruit stage the roots of Thalictrum minus L. contain d-glaucine. The latter has been identified as O-methylthalicmidine.

5. The structure of thalicmidine is that of 2,3,5-trimethoxy-6-hydroxyaporphine.

6. Mellophanic acid and phenanthrene have been obtained from N-acetylthalicmine, which is neither optically active nor basic.

7. Repeating the Hofmann decomposition reaction of thalicmine twice yielded trimethoxymethylenedioxyvinylphenanthrene.

8. Thalicmine is a derivative of pentahydroxyaporphine. Its structure is apparently that of 3,4,7-trimethoxy-5,6-methylenedioxyaporphine.

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Received October 17, 1950

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* See Consultants Bureau translation, p. 1197.

THE ALKALOIDS OF *HAPLOPHYLLUM PERFORATUM*, *H. PEDICELLATUM*, *H. DUBIUM*, *H. BUCHARICUM*, AND *H. VERSICOLOR*. I.

S. Yunusov and G. P. Sidyakin

The genus *Haplophyllum* A. Iuss. (*Rutaceae* family) embraces 32 species of plants that grow on the territory of the Soviet Union, 23 of them being found in Central Asia, including 14 in Uzbekistan [1]. The *Rutaceae* family includes the thoroughly investigated *Citrus* genus and the *Pilocarpus jaborandi* plant, which contains the valuable alkaloid pilocarpin. Representatives of the *Haplophyllum* genus, however, have remained practically unexplored chemically. All we have is some information on the approximate alkaloid content of some species in this genus [2], and the report that the alkaoid haplophylline $C_{16}H_{23}NO_4$ has been isolated from H. Sierversii [3]. We have been unable to find any further information on this alkaloid in the literature. Research on the alkaloid-containing species of the *Haplophyllum* genus is, therefore, of indisputable interest. With this in mind, we set as our objective an investigation of the *Haplophyllum* species that grow on the territory of Central Asia [4].

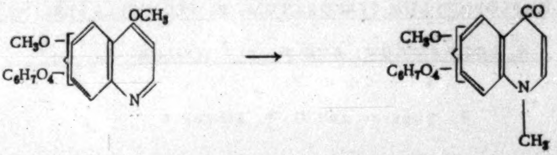
A 1948 botanical expedition of the Institute of Chemistry of the Uzbek Academy of Sciences, headed by E. E. Korotkova (and with one of the present authors as a member – G.P.S.), discovered and collected several alkaloid-containing species of the *Haplophyllum* A. Iuss. genus in the Kashka-Darya and Surkhan-Darya regions of Uzbekistan. We made the most detailed analysis of the plant *Haplophyllum perforatum* (M.B.) Kar. et Kir. (synonyms *Ruta divaricata* Siev., *H. Sieversii*, Fisch). We also began a study of the alkaloids in *H. pedicellatum* Bge. (synonyms *H. hirsutum* Rgl. et Schmalh., *H. pilosum* Franch.), *H. dubium* Eug. Kor. (synonyms *H. Albertu Regelii f. subternata* Eug. Kor.), *H. bucharicum* Litv. (synonym *H. nigripes* Nevski), and *H. versicolor* Fisch. et Mey (synonyms *H. lasianthum* Bge, *H. hispidulum* Bge.).

1. *H. perforatum* was collected in the vicinity of the villages Varganza and Makrida, Kitab district, Kashka-Darya region (the western spurs of the Zeravshan range, basin of the Kashka-Darya river). In this region this plant grows on the partially bare slopes of the foothills and the lower mountain zones.

The alkaloids were extracted from the leaves and the small stems of *H. perforatum*, gathered during the budding period, with dichloroethane, the bases being extracted from the latter by means of dilute sulfuric acid. When the acid solution was alkalinized with gaseous ammonia, the bases were precipitated (aqueous mother liquor "A"). The precipitate was recrystallized from benzene and then from acetone. This yielded the hydrochloride, from which the bases were recovered as microscopic needles with an m.p. of 155-156°. This base is optically inactive, freely soluble in chloroform, less so in benzene and ether, and slightly soluble in water and petroleum ether; it crystallizes from acetone (1: 15) and alcohol as minute needles. The yield was 0.075% (of the weight of the dry leaves). Elementary analysis indicated that its empirical formula was $C_{17}H_{19}NO_6$. Since this alkaloid proved to differ from all the bases described in the literature up to now, we named it haploperine.

Haploperine is a weak base, its salts hydrolyzing readily in aqueous solutions, even in the cold. It is an unsaturated compound, decolorizing permanganate in an acid medium instantaneously; it contains two methoxy groups, but no methylenedioxy group. The base does not dissolve in caustic alkalies; it forms a crystalline hydrochloride. When haploperine is heated for a long time with an alcoholic alkali, all of it is recovered unchanged. When haploperine is heated with 20% hydrochloric or 25% sulfuric acid, it yields a crystalline product – colorless needles with an m.p. of 138-139°. This product crystallizes from alcohol (1:7), is insoluble in caustic alkalies, and decolorizes permanganate in acid media; it retains both of the methoxy groups, but has no hydroxyl group. It is most likely that in this reaction one molecule of water is split off, since the elementary analysis indicates that the minimum formula of the base has been diminished by one atom of oxygen and two atoms of hydrogen. The mother liquors contained no other products besides the substance with an m.p. of 138-139°.

Haploperine is not affected by boiling with methyl iodide. But when it is heated in a sealed tube immersed in a boiling water bath, it is converted into an isomeric compound, which we have named isohaploperine. The composition of the latter is $C_{17}H_{19}NO_6$.. Analysis indicates that this compound, in contrast to the original base, contains only one methoxy group. This behavior is typical of γ-methoxyquinolines, which are thus converted into N-methyl-γ-quinolones [5]:



This reaction enables us to postulate roughly that haploperine is a deivative of quinoline, in which one of the methoxy groups is at the gamma position. The position of the second methoxy group is still unknown. Thus, the formula of isohaploperine must look like this: $C_{14}H_{13}O_4(>CO)(>N-CH_3)(-OCH_3)$.

The alkaloids galipine, cusparine, dictamnine, and skimmianine and other quinoline derivatives undergo similar transformations [6,7].

Isohaploperine is freely soluble in acetone and alcohol, less so in benzene, and slightly soluble in ether, petroleum ether, and water; it crystallizes from methanol (1:6) as large needles, M.p. 158-159°.

As stated above, haploperine is an unsaturated compound; when the base is hydrogenated by the Adams method, its molecule adds 6 hydrogen atoms, turning into hexahydrohaploperine $C_{17}H_{25}NO_6$, a crystalline product with an m.p. of 159-160°. Its mixed melting point with the base exhibited depression. Hexahydrohaploperine is freely soluble in chloroform and acetic acid, less so in alcohol, and slightly soluble in water, ether, and petrolem ether. We were unable to obtain crystalline salts of this substance under the conditions usually employed.

The alkaloids were extracted with chloroform from the aqueous mother liquor "A" left after the haploperine had been thrown down. Driving off the chloroform left behind a dark noncrystallizing oil, from which the alkaloids were extracted by a hot mixture (1:3) of acetone and petroleum ether. The solvent was driven off, leaving a crystalline mass mixed with a yellow oil. The latter was washed out of the crystals with ether. The crystals had an m.p. of 175-176° after recrystallization from methanol (1:5). Recrystallizations from benzene (1:15) and from acetone did not affect the melting point. We secured a picrate with an m.p. of 195-197° (with decomposition). The empirical formula of the base is $C_{14}H_{13}NO_4$. All these findings fully agree with the properties and the composition of the alkaloid skimmianine, which was first isolated from the leaves of Skimmia japonica Thunb. (Rutaceae family) by Honda [8]. Since we had no sample of skimmianine, we unfortunately could not compare these two bases directly, but the data cited above convinces us that they are identical.

After the skimmianine had been precipitated, we were able to secure a small quantity of a base No. 3, with an m.p. of 110-111°, from the mother liquor by means of crystallization from petroleum ether. When enough of this base has been accumulated, it will be analyzed in greater detail.

H. perforatum was gathered at various times: during the budding period (May 13-15), the full-blooming period (June 1-5), and the fruit-bearing period (July 17-19), in order to determine the dynamics of the accumulation of alkaloids [9] in various organs of the plant as a function of the period of vegetation. Each vegetative organ was crushed and moistened with 5% ammonia, the alkaloids being extracted with chloroform in a Soxhlet apparatus. It was found that most of the alkaoids are located in the leaves, only a slight amount being found in the stems. But even in the leaves the quantity of alkaloids varies with the time at which they are gathered, the alkaloids totalling 0.1% of the dry leaf weight during the budding period, 0.4% during flowering, and 1.2% when the seeds begin to ripen. The leaves do not fall after the seeds have ripened, continuing their living activity, but we did not investigate the alkaloid content during this period or after the above-ground part of the plant had died off.

The percentage of alkaloids in the stems varies as follows: it is 0.14% (of the dry stem weight) during the budding period, 0.1% during flowering, and 0.075% during the fruitbearing season. During this latter period we also analyzed the roots, finding they contained 0.025% of alkaloids. The highest percentage of alkaloids were found in the seeds – 1.6%. The seeds were also found to contain oil.

The percentages of haploperine and of skimmianine in the total alkaloids varies greatly with the developmental period and the respective organ of the plant. During the budding season the principal alkaloid extracted from the leaves is haploperine (63% of the total). The percentage of haploperine then decreases, being 8.3% of the total alkaloids during the period when the fruit ripens. The percentage of skimmianine, on the other hand, rises from a negligible figure during the budding season to 33% in the flowering stage and 66.7% (of the total weight) in the stage when the seeds ripen.

2. The above-ground parts of H. pedicellatum, gathered during the flowering period (May 5-9) in the Chirakchin and Kitab districts of the Kaska-Darya region contained 0.3% of alkaloids. The total crystalline alkaloids were extracted by the customary dichloroethane extraction. The alkaloid total was treated in the cold with 15 times its weight of acetone. An insoluble residue was left, which proved to be skimmianine. The acetone was driven out of the mother liquor to dryness, the residue being recrystallized repeatedly from dilute (1:1.5) alcohol. This yielded a base with an m.p. of 140-141°, whose elementary analysis indicated its formula was $C_{13}H_{11}NO_3$. Since this base was a new alkaloid, not described in the literature before, we called it haplophine.

3. An alkaloid mixture totaling 0.1% of the plant weight was extracted with dichloroethane from H. dubium (in the flowering stage). Part of the mixture is slightly soluble in cold alcohol. Crystallization of this portion from methanol or petroleum ether yielded a base with an m.p. of 95-96°. This base is freely soluble in ether, acetone and benzene and less so in alcohol and petroleum ether, and yields a crystalline nitrate with an m.p. of 157-158°.

4. H. bucharicum contains about 0.1% of alkaloids (in the flowering stage). The alkaloids were divided into two parts according to their solubility in a hot mixture of ether and petroleum ether. As the soluble portion cooled, skimmianine settled out. Recrystallization of the insoluble part from methanol yielded a substance with an m.p. of 151-152°.

5. 0.011% of an alkaloid mixture was extracted from the above-ground part of H. versicolor (during the flowering period).

EXPERIMENTAL

1. Haplophyllum perforatum

Extraction of an alkaloid mixture. The leaves of H. perforatum, with buds and small twigs, totaling 80 kg gathered during the budding period, were wetted down with 10% ammonia, and the alkaloids were extracted with dichloroethane. The alkaloids were extracted from the dichloroethane with 10% sulfuric acid. Saturating the acid solution with ammonia threw down a flocculent precipitate of technical haploperine. The yield totaled 60 g. The alkaloids were extracted from the aqueous mother liquor "A" with chloroform; driving off the latter left a thick, dark oil. 35 g yield. A total of 95 g of the mixture was obtained, or 0.1% by weight of the dry leaves containing buds and small twigs. The haploperine was refined by recrystallizing it once from benzene and then three times from acetone (1:15). M.p. 155-156°.

0.1066 g substance: 0.2410 g CO_2; 0.0590 g H_2O. 0.1014 g substance: 0.2292 g CO_2; 0.0576 g H_2O. 0.1096 g substance: 4.2 ml N_2 (15°, 729 mm), 0.1140 g substance: 4.4 ml N_2 (14°, 729.37 mm). 0.0229 g substance: 8.3 ml 0.1 N $Na_2S_2O_3$ (Viebock). 0.0228 g substance: 8.2 ml 0.1 N $Na_2S_2O_3$. Found %: C 61.69, 61.68; H 6.19, 6.36; N 4.27, 4.31; CH_3O 18.9, 18.39. $C_{17}H_{19}NO_6$. Calculated %: C 61.26; H 5.70; N 4.20; $2CH_3O$ 18.73.

Haploperine hydrochloride. An alcoholic solution of hydrochloric acid was added to 1 g of the base in 10 ml of absolute alcohol until the reaction to Congo red was weakly acid. To this solution 20 ml of ether was added. Overnight minute crystals of the hydrochloride settled out; they were suction-filtered and washed with a (2:1) mixture of alcohol and ether. The yield was 1.2 g. M.p. 124-126° (with decomposition). The m.p. was raised to 129-131° (with decomposition) by triple recrystallization from alcohol (to which ether had been added). The hydrochloride was freely soluble in water, but it hydrolyzed within a few mintues in aqueous solution, the base settling out as a precipitate. Adding 10% ammonia to an aqueous solution of the hydrochloride threw down the base, which was recrystallized twice from acetone (1:15). M.p. 155-156°.

Action of hydrochloric and sulfuric acids upon haploperine. 1 gram of the base was dissolved in 10 ml of 20% hydrochloric acid, and the solution was heated on a water bath for 2 hours. Then it was chilled, and 20% ammonia was added until the reaction was alkaline. A thick, faintly colored oil settled out. The aqueous solution was removed, and the oil was washed twice with water, after which it was triturated with 5 ml of ether.

Minute, slightly grayish crystals settled out; they were suction-filtered, washed with ether, and dried in vacuo. The yield totaled 0.8 g. M.p. 123-125°; the mixed melting point with the original base was 113-115°. The m.p. was raised to 138-139° by triple recrystallization from alcohol (1:7). The action of 25% sulfuric acid upon 1 g of the base, using the same procedure as before, yielded 0.6 g of a crystalline substance, which proved to be the same as the product secured by the hydrochloric acid treatment. We were unable to isolate any other reaction products.

0.112 g substance: 0.2658 g CO_2; 0.602 g H_2O. 0.1262 g substance: 0.3006 g CO_2; 0.0672 g H_2O. 0.0798 g substance: 3.2 ml N_2 (16°, 725.9 mm). 8.685 mg substance: 0.346 ml N_2 (23°, 736 mm). 0 226 g substance: 8.5 ml 0.1 N $Na_2S_2O_3$ (Viebock). 0.0223 g substance: 8.3 ml 0.1 N $Na_2S_2O_3$. Found %: C 65.23, 65.00; H 6.06, 5.96; N 4.43, 4.45; CH_3O 19.13, 18.94. $C_{17}H_{17}NO_5$. Calculated %: C 64.76; H 5.39; N 4.44; $2CH_3O$ 19.55.

Isohaploperine. 1 ml of methyl iodide was added to 1 g of the base dissolved in 30 ml of acetone, and the mixture was boiled for 6 hours on a water bath. The solution was filtered and concentrated to 5 ml. Minute crystals, which turned out to be the original base, settled out overnight. 1 gram of the base was mixed with 2 ml of methyl iodide (using no solvent), and the mixture was heated on a boiling water bath in a sealed tube for about an hour. The base began by dissolving, crystals appearing on the walls of the tube as heating continued. The contents of the tube solidified completely upon cooling. The tube was opened, and the residual methyl iodide was driven off, leaving a solid, faintly colored residue. The yield was 1.0 g. The isohaploperine produced was dissolved by heating it in 6 ml of methanol, large needles settling out when the latter cooled. Recrystallization was repeated three times, after which the isohaploperine had an m.p. of 158-159°; its mixed melting point with the original base was 132-134°.

0.242 g substance: 4.8 ml 0.1 N $Na_2S_2O_3$ (Viebock). 0.0252 g substance: 4.9 ml 0.1 N $Na_2S_2O_3$. Found %: CH_3O 10.09, 9.90. $C_{17}H_{19}NO_6$. Calculated %: CH_3O 9.84.

Hydrogenation of haploperine. 1 gram of haploperine with an m.p. of 155-156° was dissolved in 20 ml of acetic acid and reduced with a platinum catalyst, prepared (by the Adams method) from 0.21 g of platinic oxide. The absorption of 205 ml of hydrogen took 1 hour and 20 minutes (67 ml of hydrogen being required for one double bond). No more hydrogen was absorbed during further shaking on the agitator. The catalyst was suction-filtered and washed with water. The filtrate and the wash waters were combined. The acid solution was alkalinized with 25% ammonia. This threw the base down as a precipitate, which was suction-filtered and washed, first with 15 ml of water, then with 3 ml of alcohol, and then with 5 ml of ether. The m.p. was 159-160° after drying in the vacuum desiccator. The yield was 0.9 g. The melting point was unaffected by recrystallization from acetone (1:20).

Hexahydrohaploperine was slightly soluble in water, ether, and petroleum ether, more readily soluble in alcohol, and freely soluble in chloroform. We were unable to secure the perchlorate, the hydrochloride, the picrate, the oxalate, the hydriodide, the nitrate, or the sulfate in the crystalline state under ordinary conditions.

Skimmianine. 35 grams of the thick oil obtained from the aqueous mother liquor "A" was boiled with 600 ml of a 1:3 mixture of acetone and petroleum ether. The solution was filtered hot; during the next 24 hours crystals mixed with a yellow oil settled out. The solvent was evaporated to dryness. 125 ml of ether was added to the residue, the crystals not dissolving, though the oil dissolved completely. The crystals were suction-filtered and washed with ether (mother liquor "B"). The yield was 6 g. Triple recrystallization from methanol (1:5) yielded large, colorless needles with an m.p. of 175-176°.

0.1062 g substance: 0.2504 g CO_2; 0.0504 g H_2O. 0.1032 g substance: 0.2442 g CO_2: 0.0502 g H_2O. 0.0928 g substance: 4.6 ml N_2 (17°, 715 mm). Found %: C 64.34, 64.57; H 5.31, 5.44; N 5.37. $C_{14}H_{13}NO_4$. Calculated %: C 64.86; H 5.0; N 5.4.

The picrate of skimmianine was prepared by mixing together alcoholic solutions of the base of picric acid, minute crystals with an m.p. of 187-188° settling out. The crystals had an m.p. of 195-197° (with decomposition) after triple recrystallization from alcohol.

Processing the mother liquor "B". The ether mother liquor "B" left after the skimmianine had been filtered out was concentrated to small volume and poured into a dish. What was left was a yellow oil, which was boiled several times with petroleum ether. Part of the oil did not dissolve. When the concentrated solution was allowed to stand, crystals settled out as elongated needles. M.p. 108-109°. Yield 0.2 g. The m.p. was raised to 110-111° (Base No. 3) after recrystallization from a 1:1 ether-petroleum ether mixture. Further refining did not raise the melting point any higher. This base was freely soluble in alcohol, acetone, methanol, ether, and benzene, and less so in petroleum ether.

2. Haplophyllum pedicellatum

Extraction of alkaloids. The alkaloids were extracted from 10 kg of the air-dry, pulverized plant in the same way as that used for H. perforatum. The alkaloids were extracted from the alkaline solution with ether and then with chloroform. The ether extract yielded 27 g of bases, and the chloroform extract 4.5 g, as a colored crystalline mass. The total base yield was 31.5 g (0.3% of the plant by weight). The mixture was triturated with a small quantity (20-25 ml) of acetone and then suction-filtered. What was left was a mixture of bases freed from tarry impurities.

Skimmianine. The purified mixture of bases was processed with 500 ml of acetone. The insoluble portion was suction-filtered and washed with acetone (mother liquor "C"). The yield was 5 g. M.p. 175-176°. Its mixed melting point with the skimmianine secured previously exhibited no depression.

Processing the mother liquor "C". Haplophine The acetone was driven off to dryness. The residue (20 g) was recrystallized 3 times from dilute alcohol (1:1.5), and from a mixture of equal parts of acetone and petroleum ether (1:20). This yielded colorless crystals with an m.p. of 140-141°. Haplophine is slightly soluble in water and in petroleum ether, more soluble in ether, alcohol, and acetone (1:15), and freely soluble in chloroform.

0.1008 g substance: 0.2520 g CO_2; 0.0484 g H_2O. 0.1076 g substance: 0.2684 g CO_2; 0.0482 g H_2O. 0.1136 g substance: 6.35 ml N_2 (17.5°, 731.9 mm). 0.1246 g substance: 7.1 ml N_2 (15.5°, 724.9 mm). Found %: C 68.22, 68.07; H 5.37, 5.01; N 6.20, 6.32. $C_{13}H_{11}NO_3$. Calculated %: C 68.12; H 4.8; N 6.11.

SUMMARY

1. Three alkaloids have been extracted from the leaves, buds, and young twigs of Haplophyllum perforatum (M.B.) Kar. et Kir.: skimmianine; a crystalline base with an m.p. of 110-11°; and the new alkaloid haploperine $C_{13}H_{13}NO_4(OCH_3)_3$, with an m.p. of 155-156°. Haploperine hydrochloride, with an m.p. of 129-131° (with decomposition), and hexahydrohaploperine $C_{17}H_{25}NO_6$, with an m.p. of 159-160°, have been synthesized. A substance with the composition of $C_{17}H_{17}NO_5$ and an m.p. of 138-139° has been obtained by reacting haploperine with acids.

2. The action of methyl iodide upon haploperine has yielded the isomeric compound isohaploperine: $C_{14}H_{13}O_4(>CO)(>N-CH_3)(OCH_3)$. Haploperine is apparently a derivative of quinoline.

3. The alkaloids are contained principally in the leaves and seeds. The percentage of alkaloids in the leaves rises until the fruit-bearing stage is reached, while the percentage in the twigs diminishes. As the plant develops the percentage of haploperine diminishes during these periods, whereas that of skimmianine increases.

4. The above-ground part of Haplophyllum pedicellatum Bge. contains 0.3% of alkaloids during the flowering period. Skimmianine and a new alkaloid: haplophine $C_{13}H_{11}NO_3$, m.p. 140-141°, have been isolated from the alkaloid mixture.

5. A mixture of alkaloids totaling 0.1% has been extracted from Haplophyllum dubium Eug. Kor. (during the flowering period), from which a base with an m.p. of 95-96° has been isolated.

6. Haplophyllum bucharicum Litv. contains 0.1% of alkaloids during the flowering period. Skimmianine and a base with an m.p. of 151-152° have been isolated from the total alkaloids.

7. *Haplophyllum versicolor*, Fisch. et Mey contains 0.01% of alkaloids during the flowering period.

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Received October 17, 1950

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